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Yes, the December Number of the *Surgical Clinics of North America,* from Philadelphia, contains an excellent *10-clinic Symposium on Fractures.* There are clinics on Fractures of the Pelvis, Fracture of Upper Third of Humerus, Fractures of the Carpal Scaphoid, Russell Extension, Contaminated Wounds and Compound Fractures, Treatment of Fractures at Ankle, Epiphyseal Injuries in Childhood, Treatment of Cerebral Trauma Based Upon Laws of Cerebral Hydrodynamics, Practical Fracture Physical Therapy, and Occupational Therapy in Treatment of Fractures. And the Surgeons who present this Fracture Symposium include such leaders as Eliason, Johnson, Bates, Ferguson, Ryan, Walkling, Crossan, Kaplan, Temple Fay, Murray Wright, Impink, and Lee.

But the *entire number* is a decidedly helpful presentation that contains a wealth of practical aids and guides for the Family Physician as well as for the Surgeon. For instance, in addition to the Symposium, there are clinics on Regional Ileitis, Treatment of Ruptured Appendix, Treatment of Septic Abortion, Postpartum Hemorrhage, Acute Infections of Soft Tissues of the Neck, Skin Lesions in Surgery and others equally important—equally helpful.

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THE DIAGNOSIS AND TREATMENT OF CIRRHOSIS OF THE LIVER IN ITS EARLY STAGES

CLINICAL LECTURE AT ATLANTIC CITY SESSION

THOMAS P. SPRUNT, M.D.

BALTIMORE

The intensive research dealing with the liver during the past two decades has added greatly to our knowledge of the physiology of this important structure. It has emphasized the protean nature of its activities as well as its extraordinary powers of reserve and of regeneration. In certain striking particulars this knowledge has been translated into a great increase in our clinical power, notably in the development of liver extract in the treatment of pernicious anemia. It has taught a great deal about acute diffuse diseases of the liver, and physicians are beginning to acquire more definite knowledge of that important chronic disease cirrhosis, but clinicians as yet have done little to improve their diagnostic acumen regarding the early stages of cirrhosis, in which treatment may be more effective.

In spite of increased knowledge of physiologic chemistry, the most valuable clinical data for the diagnosis of hepatic diseases are still to be obtained by a painstaking clinical history, a careful physical examination and other relatively simple methods of bedside observation. It has been pointed out repeatedly that the most obvious evidences of disease of the liver have to do with the excretion of bile, with its relation to the portal circulation and with its variability in amount. Hence the pathologic factors of jaundice, of portal obstruction and of variations in size, consistency and shape of the liver loom up importantly in bedside examinations and observations.

In many typical cases such methods will suffice, but in other cases the difficulties of differential diagnosis or the wish to make earlier diagnoses has made highly desirable the development of reliable tests of the functional capacity of the liver. Its multiplicity of functions, however, its wide functional interrelationships with other organs and tissues and its great reserve power have handicapped greatly a favorable consummation of this desire. Certainly no single, all-embracing test need be expected. Of the many methods that have been devised to test each of the known functions of the liver, only a few have come into anything like general use, and of these perhaps the more valuable in the diagnosis of cirrhosis of the liver are certain of the excretory tests.

Read in the Medical Division of the General Scientific Meetings at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 8, 1937.

DIAGNOSTIC FACTORS

A brief review of important diagnostic factors may not be amiss.

Jaundice.—One of the most important clinical signs of hepatic disease is jaundice, and the study of its pathogenesis has been instructive and stimulating. The rudiments of the present conception may be briefly stated as follows: Bilirubin, derived from hemoglobin, is brought in the circulation to the liver cells, which excrete it along with other constituents of the bile into the bile canaliculi, whence it passes down the bile passages into the intestine. Here it is changed to urobilin or to urobilinogen, a part of which is absorbed, carried back to the liver and excreted again into the bile. When the excretory function of the liver is depressed the urobilin often accumulates to some extent in the blood stream and may be excreted by the kidneys into the urine. Urobilinogenuria is hence regarded as an indication of depressed activity on the part of the liver. Rich[1] has emphasized the division of jaundice into two main types, retention jaundice and regurgitation jaundice.

In retention jaundice the bilirubin circulating in the blood stream may not all be excreted by the liver cells and accumulates in the blood. Under these circumstances the bilirubin seems to be bound in some way, perhaps to the plasma proteins, gives an indirect van den Bergh reaction and does not pass through the kidneys into the urine (acholuric jaundice). Retention jaundice associated with milder forms of injury to the liver, cloudy swelling or atrophy of cells, is due to an increased formation of bilirubin, together with a depressed excretory function of the liver, due in turn to different factors, particularly to anoxemia and to fever. This milder type of jaundice and of hepatic injury is associated with such diseases as the hemolytic anemias, congestive heart failure, malaria and lobar pneumonia, in which the injury to the liver and the retention jaundice are comparatively insignificant features of the illness.

In regurgitation jaundice, on the other hand, the bilirubin is excreted by the liver cells and then, through rupture of the bile canaliculi, escapes into the tissue spaces and blood sinusoids of the liver by reason either of obstruction of the larger bile ducts or of necrosis of the liver cells. In this case, not only bilirubin but whole bile gets into the blood stream. The bile pigment now is not bound, it gives a direct van den Bergh reaction and it is readily excreted by the kidneys into the urine (choluric jaundice). This is the type of jaundice associated with the major acute hepatic disorders and with biliary cirrhosis. Either type of jaundice may occur in the common portal cirrhosis. The careful observation of the occurrence of bile pigments in the tissues, in the

1. Rich, A. R.: The Pathogenesis of the Forms of Jaundice, Bull. Johns Hopkins Hosp. **47**: 338-377 (Dec.) 1930.

urine and in the intestinal tract and laboratory studies of the qualitative and quantitative relationships of bilirubin in the blood are valuable diagnostic features in hepatic disease.

Portal Obstruction and Water Retention.—The presence of ascites of even moderate degree and of a palpable spleen are usually obvious clinical conditions. The clinical study of the ascitic fluid, notably of the color, the specific gravity, the albumin content, estimated by means of an Esbach tube, and the cellular content, can be made in the simplest laboratory. In addition to the ascites, or even in its absence, one may find other evidence of portal obstruction in the development of collateral venous channels; dilated veins may be readily visible on the thoracic and abdominal walls, dilatation of hemorrhoidal veins may be noted, although they are not especially common with cirrhosis, and by the use of a thick barium paste esophageal varices may readily be demonstrated by roentgenography. The last-named test may well be performed early in the examination, for a positive result may suggest the inadvisability of passing a stomach tube. The presence of blood in the vomitus or in the stools may indicate the presence of esophageal varices. The marked increase in the caliber and in the number of anastomoses between the portal and the caval venous systems is of course an attempt at a compensatory process. So far as the ascites is concerned, the compensation if successful is also quite favorable. As with other attempts at pathologic adaptation, however, the adaptation is not always useful, and it may be harmful in this case in two ways, namely, in the promotion of the risk of hemorrhage from dilated and weakened veins and in the shunting of the liver out of the portal circulation, the body thus being deprived of important services on the part of the liver.

Until recently it was generally assumed that ascites in hepatic disease was due entirely to obstruction of the portal radicles within the liver and that the dependent edema sometimes noted was caused by the pressure of the ascitic fluid on the vena cava. It is now realized that ascites does not account for all the water retention. Observers have noted the occurrence of such retention in both acute and chronic hepatic disease in the absence of ascites. Jones [2] has emphasized the occurrence of spontaneous diuresis at a certain stage of acute and subacute hepatic disease; as this is followed usually by rapid clinical improvement he presented it as a valuable and favorable prognostic indication.

One probable cause of the disturbance in the fluid balance in disorders of the liver may be related to the blood plasma proteins. Several observers have noted some disturbance of the plasma proteins in various types of hepatic disease. This change is especially notable in cirrhosis, in which the total plasma proteins are reduced and particularly the albumin fraction. The globulin fraction may be less reduced, or it may actually be increased, with a resulting inversion of the albumin-globulin ratio. In several cases of cirrhosis reported the albumin content of the blood plasma was usually below 2.5 Gm. per hundred cubic centimeters. Several students of this problem believe that the hypo-albuminemia may itself be an indication of hepatic insufficiency. It does not behave like the simple loss of protein through inanition or dietary deficiencies, for Myers and Keefer [3] could not increase the plasma proteins in their cirrhotic patients by high protein diets and, furthermore, the reduction in the serum albumin bears no definite relationship to the amount of albumin lost in the ascitic fluid.

Changes in the Size, Shape and Consistency of the Liver.—These changes are of value primarily in calling attention to a pathologic change in the organ. The size of the liver in portal cirrhosis is usually increased in spite of the term atrophic cirrhosis. Particularly in the earlier stages the liver is apt to be enlarged, and its increased consistency makes this factor more readily available to the examiner. In toxic cirrhosis the liver may be definitely decreased in size. The size of the cirrhotic liver is determined not only by the disappearance of parenchymatous cells and the contraction of fibrous tissue that tend to decrease its size but by the storage of fats and the presence of inflammatory products that tend to make the organ larger.

Tests of Hepatic Function.—Tests have been devised for the study of many of the functions of the liver, including those having to do with the metabolism of carbohydrates, of proteins and of fats, its power of detoxication and its ability to excrete certain substances into the bile. Some of these tests have come into fairly general use, and this may be taken, to some extent, as a measure of their helpfulness. In view of the great reserve power in all these functions the tests are of possible importance only when lesions are widespread or diffuse throughout the liver. They usually have negative results, for example, in the diagnosis of such conditions as solitary abscess or sparsely scattered metastases in the organ.

Of the many tests, those that deal with the liver's excretory functions seem to be of most help in cases of cirrhosis. In cases of jaundice the study of the bile pigments in the urine, in the stool, in the duodenal contents and in the blood serum is distinctly helpful. The indirect and direct reactions of the van den Bergh test for bilirubin in the blood serum distinguish between retention and regurgitation jaundice. A positive van den Bergh reaction with a slight but definite increase in the serum bilirubin may reveal the presence of subclinical jaundice. By means of the quantitative van den Bergh test or the simpler icterus index test the amount of the bilirubin in the blood serum can be determined from time to time, and its increase or decrease may be of considerable value in the continued observation of a case.

In cases without jaundice, the study of the behavior of injected bilirubin indicates that it may prove to be a more delicate test than most others that have been devised. It will be noted that the substance used is one normally and constantly being excreted by the liver, and its use in an excretory test is therefore quite rational. So far the expense of the pure bilirubin and the somewhat involved technic have militated against its general usefulness.

Other excretory tests are based on the fact that several dyes (phenoltetrachlorphthalein, bromsulphalein, bengal rose) have been found that are excreted entirely or almost entirely into the bile. The dyes are also recognizable quantitatively when retained in the blood serum and are measured by colorimetric methods. Perhaps the most widely used of these tests is the bromsulphalein test. It has attained a certain popularity and is of particular value in the absence of jaundice or when the degree of jaundice is minimal. Obviously when there is marked jaundice the retention of the dye in the serum may merely parallel the degree of jaundice.

2. Jones, C. M., and Eaton, F. B.: The Prognostic Significance of Spontaneous Diuresis in Acute and Subacute Diseases of the Liver, New England J. Med. **213**: 907-918 (Nov. 7) 1935.

3. Myers, W. K., and Keefer, C. S.: Relation of Plasma Proteins to Ascites and Edema in Cirrhosis of the Liver, Arch. Int. Med. **55**: 349-359 (March) 1935.

Sometimes, however, a marked disproportion in the retention of dye is found in cases of small degrees of jaundice. In the performance of the test a dose of 5 mg. of the dye per kilogram of body weight is injected intravenously; at the end of one-half hour a specimen of blood is obtained and examined; the retention of a measurable quantity of the dye, 10 per cent or more, is considered definitely abnormal and indicative of damage to the liver.

Of the carbohydrate tests of hepatic function, the galactose tolerance test may be of aid in diagnosis of the acute injury to the liver that precedes the development of toxic cirrhosis. In cases of marked jaundice there may be difficulty in the differentiation between diffuse necrosis of the liver and the jaundice due to obstruction of the common bile duct. The galactose test is of value especially in the early stages of the illness, when the destruction of liver cells, on the one hand, is at a maximum and when, on the other hand, the damaging effect of obstruction of ducts on liver cells is still slight. Other carbohydrate tests are occasionally used in cases of cirrhosis, namely, the levulose tolerance test and modifications of the dextrose tolerance test, but they usually give positive results only in advanced cases and in general seem less helpful than the excretory tests.

Methods based on the protein metabolism of the liver have not been strikingly helpful and are not widely used. If the changes in the blood plasma protein may be considered in the light of such metabolism they may be of value in the absence of other causes of hypoalbuminemia. The study of fat metabolism in this relationship is relatively new and not yet well evaluated.

TYPES OF CIRRHOSIS

Of the several types of cirrhosis, by far the commonest is the so-called common or portal cirrhosis, and with this type I am particularly interested in this paper. Next perhaps in frequency is the type called by Mallory[4] toxic cirrhosis or cirrhosis of acute toxic origin. Of the relatively rarer types, the pigmentary cirrhoses present quite separate problems and will not be considered at this time. By biliary cirrhosis is meant a chronic diffuse hepatic disease associated particularly with chronic jaundice and due either entirely to prolonged obstruction of ducts or to the combination of obstruction and infection of ducts. This type is also relatively uncommon, and it has a certain analogy to chronic pyelonephritis as a comparatively unusual cause of renal insufficiency. In both instances the problems of prophylaxis and of cure have to do with the avoidance or the amelioration of obstruction and infection in the respective excretory channels. At times there are definite surgical implications.

In cases of well developed ordinary portal cirrhosis the diagnosis is usually easy. The abdomen is distended with fluid, in spite of which the firm edges of the liver and of the spleen may be felt. The bulging abdomen is in striking contrast to the emaciation of the body elsewhere. There are the pinched sallow face and the muddy or subicteric conjunctivae. Dilated veins on the thoracic and abdominal walls may be noted. There may be anorexia and nausea and perhaps vomiting; the tongue may be coated and the breath offensive. Hematemesis and melena may occur from oozing or rupture of an esophageal varix; there may be moderate or marked secondary anemia. Occasional spells of fever are not uncommon. The urine is rather scanty, is concentrated and contains urobilinogen. Mild jaundice may be obvious occasionally. An examination of the blood may show a positive van den Bergh reaction and a slight increase in the bilirubin content of the blood even in the absence of definite clinical jaundice. Such jaundice in cirrhosis is due not to a general obstruction of ducts, like that of a stone in the common duct, but to distortion and obstruction of small ducts here and there within the liver and may show varying degrees of severity. The blood may also show the characteristic changes in the plasma proteins. Excretory tests of hepatic function give definitely positive results. In the later stages there may be hypoglycemia, decreased fibrinogen content and all the evidences of extreme hepatic insufficiency. The earlier toxic symptoms include headache, general malaise, mild clouding of the sensorium and depression; later on delirium or drowsiness and coma are the striking features.

The cirrhosis of acute toxic origin may resemble clinically and pathologically the commoner portal type. It may develop soon or late after massive necrosis of the liver, which is survived but after which the regeneration of liver cells takes place irregularly, many areas within the organ remain collapsed and become fibrosed and all the cells in many contiguous lobules are entirely destroyed.

Hepatocellular Jaundice

A. Chemical Poisons

1. Arsenobenzol derivatives—arsphenamine, neoarsphenamine, tryparsamide, etc.
2. Quinoline derivatives—cinchophen, atophan, quinophen, phenoquin, acophanyl, hydrocin, oxyiodide, arcanol, etc.
3. Halogen group—chloroform, carbon tetrachloride, tetrachlorethane, ethyl chloride, ethyl bromide, trichlorethylene, tribromethanol (avertin).
4. Aromatic organic compounds—trinitrotoluene (T.N.T.) dinitrobenzene, dinitrophenol, picric acid, toluylenediamine and acriflavine.
5. Miscellaneous—arseniureted hydrogen, phosphorus, alcohol, lead, mercury, synthalin, snake venom.

B. Vegetable Poisons

Mushroom poisoning.

C. Bacterial or Virus Poisons

Epidemic catarrhal jaundice (infectious jaundice), pneumonia, yellow fever, influenza, food poisoning, typhoid, paratyphoid, typhus and parenteric fevers, streptococcic septicemia.

D. Protozoal Poisons

Syphilis—icterus syphiliticus praecox, specific chronic interstitial hepatitis.

Spirochaetosis icterohaemorrhagica, amebic dysentery, malaria, kala-azar, relapsing fever.

E. Miscellaneous

Idiopathic nonepidemic catarrhal jaundice (some types), toxemias of pregnancy, uremia, goiter, acidosis of recurrent vomiting in children, portal cirrhosis.

It is known from many statistical reports on autopsies that a large proportion, perhaps one half, of the patients listed as having cirrhosis of the liver died of accident or some cause other than the cirrhosis. One cannot be sure in how many cases latent cirrhosis is well compensated and the patient reasonably safe in his hepatic health and how many patients may soon acquire signs and symptoms of cirrhosis. The fact, however, emphasizes the difficulties of early diagnosis and at the same time puts the physician on his mettle in making the attempt.

ETIOLOGY

In both the prevention of cirrhosis and the diagnosis of cases in the early stages, some consideration of the etiology is essential. In the acutely developing cases a single massive destructive lesion may suffice. The widely diversified list of possible agencies in the production of such lesions may be appreciated by study of a table like that published by Bockus and Tumen[5] under the

4. Mallory, F. B.: Cirrhosis of the Liver: Five Different Types of Lesions from Which It May Arise, Bull. Johns Hopkins Hosp. **22**: 69, 1911.

5. Bockus, H. L., and Tumen, H. J.: Jaundice, in Piersol, G. M.: The Cyclopedia of Medicine, Philadelphia, F. A. Davis Company, 1933, vol. 7, p. 588.

title "Hepatocellular Jaundice," which is another name to indicate widespread necrotic lesions in the liver. In the commoner cases of portal cirrhosis with insidious onset and gradual progression there are presumably multiple small and frequently repeated insults to the liver cells, but there are no particular reasons to believe that the sources of these insults are different in kind from those capable of causing the more acute and massive lesions. In the case of acute hepatic disease there is the impression that one can divide the causes of the disturbance into direct exciting causes and predisposing causes, the direct causes being those listed in the table and the predisposing causes such factors as a depletion in the glycogen reserve of the liver, anoxemia, the presence of a preexistent chronic diffuse disease of the liver, pregnancy and the puerperium, toxic thyroid states and the presence of a syphilitic infection.

The etiologic factors in general of the insidious chronic cases are much less well understood, and one has distinct difficulty in separating possible exciting from possible predisposing causes; for example, it is believed that syphilis can directly cause the ordinary type of portal cirrhosis, and it is also believed that syphilis may be a predisposing factor in its development. Alcohol occupies a prominent place in the clinical mind as an etiologic agent in portal cirrhosis, which can quite correctly be called alcoholic cirrhosis in a large proportion of the cases, but there is no unanimity of opinion as to whether the alcohol is the directly poisoning agent or whether its chronic and persistent use predisposes the liver to damage by some other noxious substance.

The importance of syphilis and particularly of the treatment of this disease is being repeatedly emphasized now as a probable cause of cirrhosis. Statistics at present certainly do not show this relationship clearly, and some syphilographers are doubtful that the continuous treatment of syphilis over long periods (and particularly the use of arsphenamine) is an important factor in the development of chronic hepatic disease. Others, however, have repeatedly emphasized that it is, and Baldridge [6] reported that of a series of thirty-six patients with cirrhosis one third had histories of treatment for syphilis. There is general agreement that in at least 25 per cent of the patients undergoing intensive antisyphilitic therapy there is some damage to the liver. The uncertainty concerns the production of chronic disease, for it is well known that the liver can recover promptly and completely from acute lesions. As an illustration of the possible importance of both syphilis and antisyphilitic therapy to the production of chronic hepatic disease, Kellogg, Epstein and Kerr [7] reported a high incidence (19 per cent) of abnormal hepatic function as shown by an excretion test (bengal rose) in a group of ninety patients with untreated syphilis. Antisyphilitic therapy caused transitory disturbances in hepatic function in five of twenty-nine patients originally having a normal function and caused further impairment in four of eighteen patients with initially abnormal function. Patients with initially abnormal hepatic function had, they reported, an increased tendency to have untoward reactions to antisyphilitic therapy.

DIAGNOSIS

In the attempt to make a diagnosis of cirrhosis of the liver in an early stage or in a latent compensated case, one cannot expect to attain scientific accuracy except in the rare instance in which biopsy can be done in the course of a laparotomy instituted for some other cause. There is no other definitive test. It is a trite saying, though none the less true, that before such a diagnosis of probability is possible one must have such an eventuality in mind; one must entertain the idea of chronic hepatic disease when consulted by a middle aged man who is evidently chronically but mildly ill or who gives a history of prolonged chronic alcoholism or of a syphilitic infection with persistent treatment. The interest in this possibility will be enhanced by a further history of malaise, loss of weight, "dyspepsia" and perhaps one or more episodes of slight jaundice. The finding of a firm palpable liver should then put one on the qui vive for further evidences of liver damage. In the painstaking history one should inquire for the various possible etiologic factors, including chemical poisons, vegetable poisons and bacterial and virus diseases. One will inquire carefully for symptoms so vague that they may have been almost forgotten by the patient, particularly transient feelings of fatigability, of anorexia, of occasional nausea and vomiting, especially in the morning, of abdominal pain or unrest or irregularity of the bowel.

The suggestion of cirrhosis may come in a quite different way when the patient's chief complaint is of the vomiting of blood or the passing of black stools. Careful inquiry may then elicit a report of the early symptoms mentioned, or the hematemesis may have occurred with little or no warning. The hemorrhage is not often repeated within a short time, and the considerable interval that usually elapses before the development of ascites affords an opportunity for the use of modern methods of treatment before the reserve power of the liver has approached its vanishing point. In the case of a middle aged man with hematemesis or melena, think of the possibility of cirrhosis as well as of a peptic ulcer.

After a careful physical examination that may reveal an enlarged and perhaps slightly tender liver and possibly slight evidence of portal obstruction, further tests may be helpful:

The van den Bergh reaction of the blood serum may disclose latent jaundice that was not noticeable otherwise.

Urobilinogen may be present in excess in the urine.

The bromsulphalein test may show an abnormal retention of this dye in the blood serum.

The total blood proteins may be somewhat reduced in amount, although it is unlikely that the normal albumin-globulin ratio will be disturbed.

Particularly important, especially in cases in which there is a history of hemorrhage, is the x-ray examination of the lower end of the esophagus for dilated varices.

TREATMENT

In the institution of a therapeutic regimen for chronic diseases, a sine qua non is the satisfactory cooperation on the part of the patient; hence the psychotherapeutic approach, with encouragement, with full and complete explanations, must be primary. A situation arises sometimes, unfortunately, in which it seems necessary to frighten a patient and to frighten him badly before he can be persuaded to change his unhygienic habits. Unless the patient has a reasonable intelligence (not necessarily education) there is little hope of stopping the progress of the disease and building up a serviceable hepatic reserve.

6. Baldridge, C. W.: The Relationship Between Antisyphilitic Treatment and Toxic Cirrhosis, Am. J. M. Sc. **188**: 685 (Nov.) 1934.

7. Kellogg, Frederick; Epstein, N. N., and Kerr, W. J.: Hepatic Complications in the Treatment of Syphilis: II. Incidence of Hepatic Disease in Patients with Untreated Syphilis and During Their Subsequent Treatment, Ann. Int. Med. **9**: 1561 (May) 1936.

The second step is to secure the complete elimination, as far as practicable, of potentially harmful agents. Alcohol comes to mind at once, and one realizes the difficulty of persuading the addicted to abstain. One will probably have less trouble in eliminating irritating foods, such as spices, condiments and pickles, that are ordinarily included in this category.

There is difference of opinion in regard to the therapeutic course to pursue when a patient with early cirrhosis is receiving or should receive antisyphilitic therapy. Most authorities advise beginning treatment with iodides and heavy metals, with a later tentative trial of arsphenamine in small doses. Moore [8] emphasized the point that for patients without ascites the prognosis is good and for patients with ascites the prognosis is bad regardless of the type of treatment.

The diet must be adapted to prolonged use. Counsel of perfection should be mingled with judgment. Palatability and variety are important. The intake of protein may be kept down to about 1 Gm. per kilogram of body weight. Although in view of much experimental work one might wish to eliminate meat entirely, it is probably wiser to permit its use in small portions two or three times a week. Meat extracts and beef broth should be eliminated. The chief protein requirements should come from vegetables and dairy products.

Of the fats, butter and cream should be permitted to enhance the palatability of the diet. Fried foods, fat meats and vegetable oils should be omitted.

A high carbohydrate diet is essential. It is the most important single agent conducive to building up the liver's resistance and adding to its reserve. The ideal should be to keep the liver cells constantly well supplied with glycogen. It is estimated by Althausen [9] and others that the usual high carbohydrate diet will furnish from 250 to 300 Gm. of dextrose daily. A theoretical quantity of from 500 to 550 Gm. is desirable, and the additional amount may be served as pure dextrose in fruit juice between meals and before the patient retires at night. Cereals and other starchy vegetables loom large in such a diet. If there are unpleasant digestive symptoms the green vegetables may be prepared as purées. The dextrose may at times be disturbing and should then be omitted for a period or given during two days of each week.

The hygiene of rest and of exercise needs attention. The patient should avoid marked fatigue. There should be a brief period of rest, with the patient lying down, in the middle of the day, and he should spend nine hours in bed each night. Mild exercise, well within the patient's tolerance, may be permitted at once, and with improvement this should be gradually increased. Recreation and diversity of interests are thereby enhanced.

Certain accessory methods of therapy may be useful. Many physicians like to give iodides a thorough trial even in the absence of a positive Wassermann reaction or other evidence of syphilis. Small daily doses of calcium may be useful and would seem to me harmless. Certainly in some cases of more acute poisoning of the liver, such as poisoning with carbon tetrachloride, the toxicity is attributed in part to guanidine compounds and the favorable effect of calcium to its union with these substances.

There are a number of reports relating to protective methods in experimental poisoning of the liver. Cutler [10] found that no type of diet would protect the liver tissue of his experimental animals from destruction by carbon tetrachloride but that diets rich in carbohydrates and in calcium were effectual in combating the degree of intoxication and the number of deaths secondary to the hepatic damage. Forbes, Neale and Sherer [11] described an aqueous solution of an alcoholic fraction of liver that protects animals against necrosis due to administration of chloroform or carbon tetrachloride. Their report is intriguing and may hold a certain amount of promise for the therapy of human diseases.

Particular situations may demand special attention. With bleeding esophageal varices, the esophagus must be kept at complete rest by the withholding of food or water by mouth and the administration of fluid and dextrose parenterally. Transfusions of blood may be advisable later. In considering the treatment of early cases one needs not go into the treatment of ascites. Early in the development of that symptom, however, one may accomplish a greal deal by the moderate withholding of salt and of fluids and the use of ammonium chloride and mercurial diuretics such as salyrgan and mercupurin (the sodium salt of trimethylcyclopentanedicarbonic acid-methoxy-mercury-allylamide-theophylline).

Finally, a physician and his patient should have regular conferences in which the details of the treatment are discussed and the patient's confidence and cooperation stimulated by judicious admonition and encouragement.

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8. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, Publisher, 1933.
9. Althausen, T. L.: Dextrose Therapy in Diseases of the Liver, J. A. M. A. **100**: 1163 (April 15) 1933.
10. Cutler, J. T.: Influence of Diet in Carbon Tetrachloride Intoxication in Dogs, J. Pharmacol. & Exper. Therap. **45**: 209-226 (June) 1932.
11. Forbes, J. C.; Neale, R. C., and Sherer, J. H.: A Liver Preparation Protecting Against Necrosis from Chloroform or Carbon Tetrachloride Administration, J. Pharmacol. & Exper. Therap. **58**: 402-408 (Dec.) 1936.

THE LASTING CURE OF EARLY PULMONARY TUBERCULOSIS

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There are seven reasons for directing attention again to the early tuberculous lesion and its cure; to wit:

The nature of the early lesion is better understood now than ever before.

The time of life when the lesion is most likely to appear is more clearly defined.

The methods of diagnosing its presence have been developed and perfected.

The subsequent behavior of the early lesion and the ways of its healing or advancement are better known.

Most disabling and fatal tuberculosis originates in this lesion.

Knowledge of the methods of treatment and their proper selection and application is more accurate and reliable.

The far reaching and vastly superior results of proper and timely treatment of the early lesion are firmly established.

Today, as in previous decades, from 60 to 70 per cent, at least, of all tuberculous patients in this country are in an advanced stage of the disease when the diagnosis is made, their treatment is exceedingly costly in terms of money and other less tangible but more important values, and the results of treatment are, on the whole, unsatisfactory. Recovery involves a certain permanent loss of pulmonary function, a limitation of the

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usual activities of life and a danger of relapse. Could the knowledge that has come slowly through years of experience and research be applied wisely and widely, this picture could be changed almost completely for the better. The early pulmonary lesion is one of the vital and focal points for the attack.

NATURE OF THE EARLY LESION

It is obvious that the small tuberculous lesion first discovered in the lung is not necessarily an early one. The line of thought will be more direct if I start with the lesion that is not only small but also recently developed. It may be caused by infection from without or by an extension from preexisting lesions, usually tiny or even microscopic, which, for a short or long time, have lain dormant and concealed. Previous examinations, therefore, may have revealed nothing abnormal except perhaps an apparently insignificant apical scar or a calcified hilar lymph node. The development of the early lesion, often called the early infiltration, may be rather abrupt, that is, within a week or a month, or it may be gradual with static periods of apparent quiescence. Rapidity of development, however, is one of its common characteristics. Pathologically it is a patch of tuberculous bronchopneumonia, occupying a section of the parenchyma usually not more than 2 or 3 cm. in diameter, sometimes at the apex but more often just below. The patient has no symptoms or only slight to moderate constitutional ones, chiefly a loss of a few pounds of weight and a little undue fatigue. Fever is not usually detected, and cough, expectoration and bloody sputum are rare at this stage. In some cases a patch of fine râles may be heard directly over the small lesion, but more often the physical examination reveals nothing abnormal in the chest. The roentgenogram shows, as a rule, the small area of soft infiltration in one lung. Tubercle bacilli are not found in the sputum unless the lesion has caseated and broken into a bronchus, and this is not the condition at the very onset.

TIME OF APPEARANCE

Pulmonary tuberculosis has been known since Hippocrates to take its heaviest toll between the ages of 18 and 35. This relates to disability and fatality and only by inference to the time of development of the early lesion, which has been revealed more clearly in recent years through case finding surveys among apparently healthy people. No age is immune to this danger, but the peak of development has been found to be between adolescence and the late twenties. Periodic surveys among grade school pupils have not led to the discovery of many early infiltrations. In a particularly methodical study on the basis of annual examinations of a clerical force of about 10,000 women and 2,000 men between the ages of 18 and 42 at the home office of the Metropolitan Life Insurance Company, Fellows [1] found very definite trends. Between January 1932 and December 1936, clinical pulmonary tuberculosis developed in 142 previously healthy persons, of whom 83 per cent were between the ages of 18 and 27. Here, as in other studies, the incidence was relatively higher and rose to its peak earlier in young women.

DIAGNOSIS

As shown in previous studies,[2] the early lesion will be discovered in only a small minority of cases unless the disease is viewed as a community problem and organized searches for it are made periodically. The patient, having few or no symptoms of illness, does not seek the physician. Rather, the physician, in his capacity as a far seeing health officer, must seek the patient. Tuberculin testing and x-ray examination of the chest, wisely planned and applied, are indispensable parts of the diagnostic method. If the diagnosis is adequate, it will include not only a recording of the lesion but also an interpretation of its potential significance and the need for treatment. The small size of the infiltration, the lack of symptoms, and the failure to get confirmatory evidence in the finding of tubercle bacilli in the sputum often cloak the situation with a grossly undeserved aspect of innocence.

SUBSEQUENT BEHAVIOR OF THE LESION

The early infiltration may be absorbed almost completely, leaving behind a small scar, or it may spread, become caseated and liquefied at its center and ulcerate into a bronchus, whence other parts of the lung may become contaminated, the beginning of advanced tuberculosis. Absorption, if it occurs, is slow. The tendency to central caseation is a predominant one, varying in intensity and rapidity. After ulceration and excavation of the lesion occurs, the rate and extent of formation of secondary lesions vary within wide limits. Acute bilateral tuberculous bronchopneumonia may be set up within a few weeks. More often the extensions occur at irregular intervals, and gradually the case drifts into the confirmed chronic state. The eventual contamination and infection of the larynx, intestine and other related structures by the bacilliferous discharges from the pulmonary cavities is frequent.

The frequency of spontaneous healing of untreated early lesions is a matter for further investigation. The number of old apical scars discovered at autopsy testifies to the effectiveness of natural resistance in most people. But these scars may not and probably as a rule do not represent the residues of lesions as large or as acute as those I am considering and therefore should not be taken as a measure of the spontaneous healing capacity of the latter. This can be determined only by prolonged observation of untreated patients harboring such lesions. It undoubtedly varies according to many factors, including age, race, sex and complicating diabetes. According to Braun and Roulet,[3] who have recently reviewed the European literature, the most optimistic observers estimate that as high as 40 per cent of the lesion may heal completely. I am reasonably certain, after ten years of special attention to the point, that the majority of early infiltrations developing in young people (and most of them do develop in young people, as stated) progress and undergo excavation if they are not promptly and properly treated.

MOST SERIOUS TUBERCULOSIS RELATED TO EARLY LESION

Since most patients have advanced disease when the diagnosis of tuberculosis is first made, the mode of development in the individual case is usually a matter for intelligent conjecture and inference. But sufficient information has been accumulated by the pathologists and from a study of pathogenesis in the living to warrant the conclusion that most disabling and fatal tuberculosis originates from the once innocent appearing early infiltration. An appreciation of this linkage has been lacking until recent years yet is one of the most

1. Fellows, H. H.: Personal communication to the author.
2. Amberson, J. B., Jr.: Some Case Finding Principles of Practical Significance, Tr. Nat. Tuberculosis A., 30th annual meeting, 1934, pp. 204-212; Case Finding Methods for the Diagnosis of Tuberculosis, J. A. M. A. **107**: 256-258 (July 25) 1936.
3. Braun, Paul, and Roulet, André: Etude critique du Frühinfiltrat, Rev. de la tuberc. **3**: 258-279 (March) 1937.

important and basic principles in treatment and control. The conception, to be complete, includes the element of time relationships, because, as stated, the extension from the early lesion may be rapid or slow, limited or wide, continuous or discontinuous. Connecting this conception with the evidence that most early pulmonary infiltrations put in their appearance between adolescence and the late twenties, it follows that advanced tuberculosis is unlikely to develop in a person past 30 unless he has acquired a considerable lesion before this age.

METHODS OF TREATMENT

Since the tendency is for the early lesion to caseate at its center fairly rapidly, any treatment which prevents, retards or arrests this process would logically strike at a very vital point. Absorption and durable fibrosis can be expected only when caseous degeneration has not advanced greatly. Our knowledge is still too vague to permit speaking in precise terms about the many factors which stay the progress of caseation and favor healing. Clinical experience shows that they are deep rooted and include such things as circulatory tone, capillary permeability, endocrine balance, biochemical relationships and nervous, emotional and mental stability. In fact, in the presence of the early infiltration with little or no cavity formation, these general influences are of major importance and are the main basis of the rest cure. The situation is very different from the advanced case presenting a pulmonary cavity in which local mechanical factors are important and require artificial collapse of the lung to prevent further dissemination of the infection while healing proceeds. The great advantage of the rest cure in a sanatorium, especially for younger people, has been amply proved by clinical trial. The sooner and the more strictly this can be instituted, the more effective it is likely to be. In many cases the treatment of the first few weeks is the most important of all. In the case of a person under the age of 25 with an early infiltration, our practice at Bellevue Hospital is almost invariably to advise a period of strict bed rest, lasting from two to four months. Some older patients, especially those with indolent lesions of considerable standing, may be treated less rigidly pending further clinical study. The younger the person, the more labile the lesion is likely to be and the greater the need for prolonged rest. The behavior of symptoms, repeated estimation of the blood sedimentation rate and of the white cell formula, and, above all, repeated roentgenographic examinations, at first every week or two, are the most reliable guides. Consideration of the potential hazard of the lesion, as already discussed, and of the desirability of permanent recovery with the least sacrifice of function often takes precedence and dictates continuation of rest in bed well beyond the time when symptoms have subsided and the hematologic picture is normal. From six to twelve months of sanatorium care is advantageous. Most patients can then gradually resume activities, but a definite limitation of these for another year is usually necessary. Collapse or rest of the lung by pneumothorax or temporary paralysis of the diaphragm may give the necessary lift to the patient who, on rest treatment alone, does not show definite and steady favorable progress. Since these measures occasionally are attended by hazards—some great and some small—there should be a specific and positive reason for using them. They are not necessary for the satisfactory clinical cure of most early infiltrations, and, with the exception stated, there is no convincing evidence that they shorten the desired time of treatment. My experience does not lend support to the view that in these cases pneumothorax can be considered a complete substitute for rest treatment. Few, if any, young people are able under any kind of treatment to continue work without serious jeopardy to their chances of lasting recovery. The apparent economic saving too often turns out ultimately to be a loss.

RESULTS OF TREATMENT

Statistics relating to the results of treatment of early pulmonary lesions are mingled with those concerning lesions which are small but not very early. Furthermore, the failure of patients to report for diagnosis during the first stages of development of the infiltration and the hesitancy of physicians to advise treatment when they do report help to account for the relative scarcity of cases in sanatoriums. I can speak of an experience with more than 100 cases in which the lesions were actually early, since previous roentgenograms showed no disease; they occurred in young people, and observation was possible from one to ten years afterward. This is supplemented by consideration of many hundreds of other cases of rather recent origin in which the duration and course of the disease was reasonably clear though not always verifiable. The experience is not adequate for statistical presentation and I give only a considered judgment, based more on an intensive study of individual cases than on groups. Thus far, most of the untreated cases have progressed into advanced disease. Patients treated promptly and with bed rest at the start have recovered without progression of the lesion in about 90 per cent of the instances. In most of the others, advancement or relapse, if any, has been promptly detected and usually controlled by artificial pneumothorax. Considering permanence of recovery, preservation of pulmonary function and working ability after treatment, the experience has been much superior to any other plan attempted. In the Bellevue School of Nursing the record for the past six and one-half years, during which the ideal plan has been in force, is as follows: All tuberculosis appearing in student nurses has been discovered early, usually in the form of the early infiltration. Progression or relapse of the lesion in spite of rest treatment has occurred in less than 5 per cent of the cases. All who have completed treatment are able to work, and there have been no deaths from tuberculosis. The experience can be said to approximate closely the results of treatment of minimal lesions reported by Brown [4] from the Trudeau Sanatorium, despite the distinction between minimal lesions and early lesions previously mentioned.

SUMMARY

1. The early lesion of clinical pulmonary tuberculosis is usually a small patch of tuberculous bronchopneumonia in one lung. It appears most often in the ages between adolescence and the late twenties.

2. The early lesion is not often diagnosed except in periodic health examinations or case finding surveys. As a result, most cases are advanced when treatment is instituted. This can be changed.

3. The prevailing tendency of the early lesion in young people is to caseate at its center, excavate and spread. The transition to extensive bilateral pulmonary disease may be a matter of a few weeks, a few months or many years.

4. Brown, Lawrason: The Present Status of the Treatment of Pulmonary Tuberculosis, Ann. Int. Med. **10**: 147-155 (Aug.) 1936.

4. Most symptomatic, cavernous, advanced, disabling and fatal tuberculosis originates from the early infiltration.

5. Rigid and prompt treatment of the early infiltration, as it appears especially in young people, with a preliminary period of from two to four months' bed rest has proved to be the most effective in terms of lasting recovery and avoidance of advanced relapsing disease.

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THE DIAGNOSIS AND MANAGEMENT OF LATENT, SUSPECTED AND EARLY CLINICAL TUBERCULOSIS

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Methods of tuberculosis control, in large part dependent on the ability to recognize latent and early clinical tuberculosis, have been modified greatly by a better understanding of the epidemiology of the disease and by new and more accurate diagnostic aids. Use of the terms consumption and phthisis to designate pulmonary tuberculosis is very suggestive of the advanced stage in which the disease was generally diagnosed three or four decades ago. The differentiation from other chronic respiratory diseases was not made until marked deterioration of health with emaciation, weakness and dyspnea had occurred, while the hopeless outlook and the stigma attached to the disease made the physician hesitate to make the diagnosis so long as any excuse existed for failure to make it.

Since that time educational campaigns by public health agencies have resulted in recognition of tuberculosis as a contagious disease which can frequently be controlled in the individual case by suitable treatment and can be prevented from spreading to others by isolation or prophylactic care. Examination of the sputum has gradually been accepted as a valuable diagnostic aid. The possible significance of unexplained loss of weight, fatigue, persistent cough, hoarseness, indigestion, hemoptysis and pleurisy with effusion has been repeatedly emphasized and careful physical examination of individuals exhibiting these symptoms has frequently resulted in the diagnosis of tuberculosis at a relatively early stage in its clinical course.

The importance of the diagnosis of pulmonary tuberculosis through history, symptoms and physical signs cannot be overestimated, but unfortunately symptoms sufficiently severe to cause concern often lag far behind the anatomic involvement, so that the majority of patients present moderately or far advanced disease when they first seek medical attention. Physical examination also, even in the hands of skilled examiners, not infrequently fails to demonstrate extensive tuberculous lesions.

Modern methods of tuberculosis case finding employing the tuberculin test and x-ray examination have modified our conception of early diagnosis and have presented the general practitioner with a new problem; namely, the management of apparently healthy persons who present evidence of tuberculous lesions on x-ray examination. These cases are discovered in one of two ways: either through examination of contacts of known tuberculous patients or in tuberculosis surveys of groups of apparently healthy persons such as high school and college students, pupil nurses and industrial employees. Occasionally cases are found by accident when x-ray examination is made with some other purpose in mind than the discovery of a tuberculous lesion.

The importance of the contact method of tuberculosis case finding is recognized by agencies primarily interested in tuberculosis control. The prophylactic care of contacts should also be the concern of every physician who is treating a patient with pulmonary tuberculosis.

The examination of contacts to discover those who may have been infected by the patient should include the tuberculin test and x-ray examination, since it is asymptomatic or early clinical disease that is being sought. In apparently healthy individuals a negative tuberculin reaction indicates that infection has not occurred, and from a practical standpoint further examination, though desirable, is not necessary to exclude tuberculosis. X-ray examination of all contacts or at least of contacts giving a positive reaction to tuberculin should be made whenever possible. In this way lesions can be discovered before they have caused ill health at a time when they can be most readily controlled.

If x-ray films are too expensive and cannot be obtained free or at a nominal cost, or if for any other reason reliable x-ray reports cannot be obtained, the physician should not relinquish his efforts to determine the results of infection of the contacts. Fluoroscopy, if available, affords an inexpensive diagnostic aid. Recent improvement in fluoroscopic screens has increased greatly the accuracy of this type of x-ray examination. Although inferior to x-ray films, the fluoroscope will reveal the more extensive and therefore probably the more significant pulmonary lesions.

In the absence of these facilities, careful physical examination must be relied on for the discovery of lesions in their early clinical stage. Influenza, colds in the chest or unexplained febrile attacks should be regarded with suspicion and should keep the examiner on guard. Sputum, if present, should be repeatedly examined. Fatigue, loss of weight and other symptoms suggesting tuberculosis require careful observation or even prophylactic treatment.

It is in order to point out that examinations should be repeated at frequent intervals as long as contact exists. When contact is with sputum positive tuberculosis, the interval between examinations should be three months or less. If sputum is not positive, from three to six months is an appropriate interval. The first appearance of a lesion in the x-ray film may occur months after contact with the presumable source of the disease has ceased, and the lesion, when present, may progress so slowly that no symptoms occur for a further indefinite period. For this reason, periodic examinations should continue after contact is finally broken. If x-ray examination is available, two years of observation is sufficient, but if physical examination must be relied on, periodic examinations should be made for at least five years. The importance of periodic examinations requires emphasis because not infrequently contacts are examined only once. If the expense involved prohibits the making of periodic examinations as frequently as has been suggested, they should be made less often rather than stopped completely.

The survey method of case finding consists of the application of the tuberculin test and x-ray examination to groups of apparently healthy individuals in order to discover those presenting asymptomatic tuber-

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culous lesions. Students in high schools and colleges are usually chosen for this type of case finding because they are readily available and the incidence of significant lesions is sufficiently high to justify the effort. This is a phase of the tuberculosis control program that is becoming more and more widely employed and in which the family physician should play an important part. A questionnaire sent to twenty-five of the largest cities in the United States in November 1936 revealed that nineteen had some plan for the control of tuberculosis in high school pupils already in operation while in several others plans were contemplated or larger plans were in effect, including high school pupils but not especially applicable to them.

In most tuberculosis surveys the observations are reported to the family physician or to the parent with the advice that he consult the family physician about the report. The reporting of positive tuberculin reactions without x-ray examination often results in needless worry to parents and it is doubtful whether surveys employing the tuberculin test are justified unless provision is made for continuation of the examination. The positive tuberculin reaction indicates tuberculous infection, but x-ray examination is necessary to determine whether or not the infection has resulted in a significant lesion. When a tuberculous infiltration is reported, the tendency on the part of the physician is to reassure the worried patient or his agitated parents and in some instances, unfortunately, the reassurance takes the form of denying either the existence of the lesion or its significance. This opinion is usually given after a physical examination which fails to reveal an abnormality. It must be accepted as a fact that apparently healthy persons may have potentially serious tuberculous disease and that many of those who develop tuberculosis have been strong and robust before the onset of symptoms at a time when x-ray examination would have revealed an active tuberculous lesion. The failure of the physician to recognize the limitations of physical examination and the value of x-ray examination is harmful both to himself and to the tuberculosis case finding program.

In determining the proper advice to give to a patient with latent or early clinical tuberculosis, the family history, the age of the patient, his physical condition and his social status should be considered. Since tuberculosis is a contagious disease transmitted chiefly through contact in the household, the family physician is the person who is best fitted to assume the responsibility for the management of the patient. When patients have tuberculous lesions without symptoms or physical signs, x-ray examination, as already pointed out, must be relied on as a guide to treatment and the physician should understand the type and significance of the lesion with which he is dealing.

The susceptibility to disease and the type of tuberculous lesion that most commonly occurs vary with age. In infancy, symptoms and physical signs on which a diagnosis of tuberculosis may be based do not occur until the disease is far advanced or until one of the severe and usually fatal forms of dissemination, such as tuberculous meningitis or miliary tuberculosis, has set in. For this reason the tuberculin test is of special importance in apparently healthy infants who have been in contact with sputum positive tuberculosis. If the tuberculin test is positive, x-ray examination should follow, and if a lesion is found, isolation in a hospital is indicated. When the contact is broken and the child has been placed under favorable conditions the prognosis is not hopeless unless the disease is already far advanced. Even at this age, pneumothorax treatment in unilateral or predominantly unilateral cases may be employed. The lesion found at this age is usually a tuberculous bronchopneumonia or tuberculous pneumonia in the form of consolidation of one or more lobes or parts of one or more lobes. The lymph nodes at the root of the lung are usually enlarged and caseous.

Between the ages of 2 and 12 years the typical lesion found by x-ray examination is the calcified pulmonary nodule with associated calcified focus in the tracheobronchial lymph nodes. Calcification of tracheobronchial lymph nodes recognizable in chest films is not progressive and does not cause ill health but indicates severe exposure to tuberculosis during childhood, which exposure may be continued into adolescence, resulting in the development of a lesion of adult type. Again a second exposure to tuberculosis from a new source of contagion is more likely with these children, since tuberculosis is characteristically a household disease. All members of the households of children exhibiting tracheobronchial calcification should be examined in an effort to locate the source of contagion and other individuals who may have been infected from it.

Calcification may be regarded as evidence of healing, and it is only when calcification has set in that tuberculosis of the tracheobronchial lymph nodes is ordinarily diagnosed. The presence of a calcified focus in the nodes, while leading to a diagnosis of tuberculosis, indicates a condition that is less threatening to health than the caseous focus that preceded it.

Because they do not differ in density from normal structures at the root of the lung, caseous foci in the tracheobronchial lymph nodes, unless very large, cannot be diagnosed and are disregarded. Occasionally the caseous lesion is so large that the nodes encroach on the lung field and in the x-ray film cast a shadow that extends beyond the normal hilus shadow. Here the lesion is discovered at a time when there is no evidence of healing and the possibility of progressive tuberculosis is greatest. The condition must be differentiated from other causes of lymph node enlargement. A history of contact with tuberculosis and a positive tuberculin reaction are suggestive of tuberculosis but do not exclude it by their absence. A complete blood count is indicated as well as examination for enlarged spleen and lymph nodes in other areas. The prognosis in this type of tuberculosis is good in white children if contact is broken. The nodes decrease in size, and calcification may occur.

In the age group under discussion, nonapical pulmonary infiltrations due to tuberculosis of childhood type also occur. The majority do not progress into clinical disease but largely clear, leaving only a few strands in the x-ray film. Lesions of this type that progress must be differentiated from chronic nontuberculous pulmonary disease. The nontuberculous lesion is almost always basal, is often bilateral and is usually accompanied by numerous medium and coarse moist râles. A history of pneumonia, particularly if recurrent, of frequent colds with long continued cough or the presence of infected adenoids or infected accessory sinuses is common, while with severe lesions large quantities of sputum may be expectorated. When the disease is of several years' duration the symptoms are usually much more marked in the winter and slight or absent in the summer. X-ray examination shows that the nontuberculous lesion is most intense near the borders of the heart, which are blurred, and just above the diaphragm, the shadow of which is usually irregularly peaked and blurred near the spine. The tuber-

culous lesion can usually be suspected by a history of contact. The tuberculin reaction is positive. Physical signs, including râles, are not marked. Until late in the disease x-ray examination shows that the lesion is usually unilateral or predominantly unilateral and is frequently situated anteriorly, often in the right middle lobe. Severe symptoms and positive sputum do not occur until the disease is far advanced.

Tuberculosis is sometimes suspected in children of elementary school age owing to the presence of underweight and fever. It is sometimes forgotten that the temperature in children is about 1 degree F. higher than in adults and may reach 100 F. or more without any detectable cause. Underweight has been shown by a number of studies to occur with about equal frequency in tuberculin negative and tuberculin positive children. It should not be considered as a symptom of tuberculosis unless a significant tuberculous lesion can be demonstrated.

Adult type tuberculosis is the chief cause of death between 15 and 45 years of age. The adult type of lesion rarely occurs before puberty but it is found during adolescence with increasing frequency as age advances. For this reason special attention should be given to adolescents and young adults who are in contact with pulmonary tuberculosis. Surveys indicate that apical infiltrations are demonstrable by x-ray examination in about 1 per cent of tuberculin positive boys and 2 per cent of tuberculin positive girls of high school age. The lesion may be present for months or years, as shown by x-ray examination, before it causes symptoms and physical signs. In many instances the lesion becomes scarred and inactive without treatment and without ever having been clinically manifest.

X-ray examination is necessary to determine the site, extent and characteristics of a latent apical infiltration. The tuberculin reaction is positive with few if any exceptions. With more extensive lesions, abnormal physical signs may be detected. Diminished expansion and diminished resonance on the affected side are the earliest physical signs. Crepitant and subcrepitant râles at one or both apexes heard on breathing and increased after cough, or heard only after cough, constitute the most reliable physical sign. The physical changes are complicated by anatomic differences in the two apexes. On the right, owing to the smaller apex and the position of the trachea, resonance is diminished, the breath sounds tend to be bronchovesicular and the voice sounds are louder than on the left. For these reasons tuberculous infiltration is often suspected at the right apex. Mild degrees of scoliosis and changes in the position of the subject, particularly in children, also give slight variations in physical signs. It must be recognized that unmistakable physical signs are rarely present in the early lesion, so that slight but persistent abnormal changes should be regarded with grave suspicion.

Very careful attention should be given to the symptoms of adolescents and young adults who are in contact with tuberculosis or who are known to have apical infiltration. So-called grip or influenza, pain in the chest, hemorrhage, cough or any other local or general symptom may indicate the onset of clinical tuberculosis.

The management of latent and early clinical tuberculosis should follow well recognized principles. One of the most important considerations is the prevention of further infection.

If the source of disease is not known, every effort should be made to find it. Examination of all members of the household or others with whom the patient has been in contact should be made. Owing to the chronic nature of tuberculosis, the original infection may have occurred months or years before the lesion is discovered. On the other hand, the source of contagion may be an unrecognized case of tuberculosis with which the tuberculous patient is still in contact.

If the origin of disease is known, isolation of the sputum positive case in an institution or removal from the household of the contact with latent or early clinical disease is recommended. If this is not feasible, well known prophylactic measures with regard to cough, to disposal of sputum, to care of dishes and linen and to personal conduct should be observed by all concerned. The physician should inform the patient and family about the danger of contagion or provide written instructions, which are often very helpful.

The physician who is caring for persons in contact with tuberculosis, whether or not they have a tuberculous lesion, should safeguard their health by advice calculated to promote proper hygienic habits. It is reasonable to suppose that attention to these precautions will often prevent the development of a significant lesion.

In addition to periodic examinations for contacts, patients without known contact who exhibit asymptomatic lesions should be kept under observation until it is certain that the disease is not progressive. The type and extent of the lesion are important factors in deciding the frequency with which reexaminations should be made. If the lesion when first seen is of slight extent and its appearance suggests that it has already undergone retrogressive changes, that is, calcification or scarring indicated by a strandlike appearance in the x-ray film, yearly examinations, in the absence of contact, are sufficient. Infiltrations that are not strandlike require examinations at much more frequent intervals, probably every three months, until they undergo favorable changes. In all instances examinations should be continued until the infiltration has a strandlike appearance that does not change during a period of at least three years.

In patients with latent and early clinical tuberculosis the type, extent and clinical manifestations of the lesion determine the treatment that is necessary to control the disease. Rest is the principal factor in treatment, and in many instances partial or complete restriction of activities is indicated.

In a large group, however, in addition to periodic examinations and prevention of continued infection, nothing more is indicated than an ordinary routine including the rest, exercise, nourishment and hygienic habits calculated to promote good health in normal persons. Continued observation of this type without additional restriction of activities is indicated for tuberculosis contacts with no demonstrable tuberculous lesion, for preadolescent children with calcified childhood type lesions or strandlike nonapical infiltrations, and for adults with asymptomatic apical lesions, strandlike in the x-ray film.

Partial restriction of activities is indicated for patients with asymptomatic lesions that show no evidence of healing. The modified regimen for these patients includes from ten to twelve hours in bed each night, with a rest hour in the afternoon if possible and extra rest on Sundays and holidays. Strenuous work and exercise are forbidden as well as exertion to the point of fatigue. Three good meals daily should be taken, with extra nourishment if underweight is present.

The patients put on this routine include children with uncalcified lesions of the tracheobronchial lymph nodes demonstrable in x-ray films or nonapical infiltra-

tions that are not strandlike on x-ray examination and adolescent children with apical infiltrations. In the latter, the lesion which has occurred recently should not be regarded as inactive and an altered regimen is indicated, no matter how trivial it may appear to be. Apical infiltration in young adults, unless slight in extent and strandlike in appearance on x-ray examination, also makes an altered regimen desirable.

Patients with more advanced lesions should take sanatorium treatment or its equivalent in bed rest at home. In some instances collapse therapy is indicated in addition. All patients with tuberculosis with symptoms or physical signs should have the advantage of sanatorium treatment regardless of the extent of the lesion or the character of the symptoms. In addition, patients with latent disease whose lesions progress under observation or under an altered regimen are equally in need of sanatorium treatment.

The final success of the method of tuberculosis control through early diagnosis depends on the application of adequate treatment to the progressive lesion either while it is still asymptomatic or immediately after it becomes clinical. The chief emphasis of recent educational campaigns has been placed on early diagnosis. Both the medical profession and the public now require education in the need for early treatment of tuberculosis when there has been slight or no impairment of health.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. AMBERSON AND HETHERINGTON

DR. BRUCE H. DOUGLAS, Detroit: Dr. Amberson has said that a person past 30 is not likely to develop serious tuberculosis unless he has acquired a definite lesion before that age. While this is quite true and is well supported by the experience among the nurses which he has reported and is further supported by the work of Fellows, still there is the danger that some of us may fall into a sense of false security and forget that this is a qualified statement subject to definite exceptions. Recently a man aged 62, who had had repeated negative chest films, came to the hospital with acute tuberculosis and died within six weeks. Further this line of reasoning is apt to result in programs like the following: Certain communities are examining school teachers regularly, all positive reactors to tuberculin being roentgenographed every year. If nothing is found by the age of 25 the examinations are discontinued on the basis that serious tuberculosis is not likely to appear after that age if the patient has a clear chest up to that time. Dr. Amberson of course would say 30 years, but even then I am sure he agrees that there are some who will develop disease even after that age. I agree that treatment of these early lesions is imperative. These patients need all the bed rest that Dr. Amberson has outlined as necessary. However, in our service rather than just assigning these patients to bed rest alone, it is felt that additional valuable rest for the lung can be obtained by the use of a temporary phrenic paralysis. This procedure does not interfere with good visualization of the lesion and yet adds a definite rest factor. If after a month or more observation on the program of bed rest with a phrenic crushing the disease should show progress to more serious proportions, pneumothorax should be employed. The seriousness of these early lesions cannot be too greatly stressed.

DR. CHARLES H. COCKE, Asheville, N. C.: One of the outstanding epidemiologic triumphs of medicine today is the gratifying drop in the death rate from tuberculosis. Honesty, however, compels the admission of the facts (1) that modern medicine is not altogether responsible for this drop and (2) that the morbidity of the disease has not shown a similar loss; and the further fact that in certain age groups, notably women from 15 to 30 years old, tuberculosis is still the greatest single cause of death. The explanation of this paradox I feel resides in our lack of knowledge of the exact incidence and the degree of infection in the second, third and possibly fourth decades of life. Much has been learned of the incidence of infection in school and college groups, student nurses and such related controllable groups, but so far no one has evolved a solution at once economically possible and scientifically sound for application of our known methods of detection of tuberculosis to the entire population. When health preserved becomes as precious as health lost and the same efforts and funds are available to attain this end, perhaps we shall be somewhere near, or at least nearer, the solution of the problem of tuberculosis. I am delighted to commend Dr. Amberson's stand for the prolonged treatment of the early lesion, as well as his method of treatment. In the present wave of enthusiasm for compression and surgical procedures in the treatment of tuberculosis it is well to reiterate that surgical intervention does not cure tuberculosis any more than a splint cures a fracture, that all such measures are but means to an end of assisting nature to do what we as yet have not had the wit to accomplish by pharmacologic, chemical or serologic agents—cure tuberculosis. The only known specific, as has been preached for years, is rest, and yet this means many things to many minds. One of the greatest paradoxes of the disease is the disparity between symptoms, physical observations, and roentgen appearances. The solution can be reached I feel only by an evaluation of a fourfold approach to the problem: historical (which cannot be too greatly emphasized), physical (which may be fruitless but frequently lends suspicion in some minutiae), roentgenologic (which is still our mainstay and most valuable help), and laboratory studies (which aid greatly in evaluation of the process discovered by the other measures).

DR. FRANCIS M. POTTENGER, Monrovia, Calif.: It is unfortunate, in dealing with tuberculosis, that health boards and specialists devise plans for examination and diagnosis which fail to give the general profession an intimate part in the program. Medical men in general should take the same interest in tuberculosis that they do in diseases of the heart, kidney and blood, for tuberculosis is a part of general medicine. There is neither mystery nor magic in its diagnosis. Any well trained physician can carry out the three simple measures of greatest value in diagnosis: (1) take a careful history, (2) have the sputum examined and (3) have a roentgenogram of the chest made. By making early diagnoses and at least understanding the principles of treatment, they can render as great a service to the tuberculous patients as to those suffering from other diseases. The reason specialists are dealing so constantly with far advanced tuberculosis is the fact that general medical men have largely excluded tuberculosis from their practice and failed to accept responsibility for it. They can and must accept the responsibility at least for diagnosis. We must not let the fact that specialists have devised means whereby they are able to produce healing in far advanced cases militate against early treatment. Far advanced patients are more or less handicapped for the future, and their treatment is unnecessarily expensive in both time and money. The only patient who can get well regularly and be fully competent is the one with the early or limited lesion. Dr. Amberson's point of view is sane. In private practice I make it a rule not to use any mechanical measure which carries with it the possibility of injury to the patient's respiratory mechanism unless I deem it necessary to his cure. In my relationship to indigent patients, however, I accept the necessity of interfering more frequently, because of the limited facilities for treatment at hand. Statistical proof is necessary, however, before one can be certain that it is the best practice. Nearly all patients with limited infiltration in the lung can be restored to health by physiologic treatment alone. An important factor in determining the character of treatment to be employed, as well as the permanence of results, is the environment in which patients live, both during and after treatment. The case is very different for those who go back to a bad environment as compared with those whose surroundings are favorable. Those who treat tuberculosis are obliged, unfortunately, to handle the material that comes to them, regardless of the extent of the disease, with the facilities with which they are provided, whether it is best clinical practice or not. There is danger, however, that results obtained under unfavorable conditions will influence one to advocate the same method under all conditions.

DR. S. A. SAVITZ, Philadelphia: It cannot be sufficiently emphasized that early diagnosis of tuberculosis at the present time is the most important procedure in controlling the disease. Great strides have been made in the treatment of advanced cases. Artificial pneumothorax, thoracoplasty and phrenicotomy are in a great measure responsible for the reduction of the mortality. Just as soon as the diagnosis is made at the very onset of the disease, the incidence and mortality will be reduced tremendously. It is strange that many of our present day trained physicians wait for pronounced symptoms, such as fever, cough and expectoration, even to suspect pulmonary tuberculosis. What is wrong? They are getting the best training in physical and clinical diagnosis from the freshman to the senior years; they are taught to correlate and evaluate symptoms and physical signs, they serve an internship in hospitals and attain practical experience to make them able men. Nevertheless many fail to diagnose tuberculosis at its early stage. I believe the principal reason is carelessness. At the Philadelphia General Hospital, where we house about 400 tuberculous patients, over 50 per cent on admission give a history that they have been treated for colds or something else not related to tuberculosis. I do not think that more headway will be made in the future until specialists properly instruct the general practitioner to be more careful and also instruct people in general to take better care of themselves. Periodic health examinations with an effort to diagnose tuberculosis in its incipient stage and our present day knowledge of thoracic surgery will, in my opinion, reduce the mortality and incidence of the disease to a minimum in the next ten years.

DR. SAMUEL FRIEDMAN, New York: Some patients with early or moderately advanced tuberculosis are not distressed by a cough sufficiently to call it to the attention of the doctor. When asked about a cough they may even answer "No." Particularly is the absence of a complaint about a cough true if the patient is suffering also from an associated painful disease, such as gastric or duodenal ulcer or renal or cardiac pains, the symptoms of which are so distressing as to mask the little annoyance of a slight cough or expectoration. Such early uncomplicated cases of tuberculosis are frequently overlooked or the patients are treated for bronchitis, and if this is associated with another distressing disease, are treated only for the symptoms of the annoying coexisting disease. It is necessary never to ignore a slight or moderate persistent cough or expectoration. It is most advisable at times to stress the question. X-ray and sputum analysis, and a tuberculin test, when in the slightest of doubt, will save many a regret. On the other hand, it must also be borne in mind that there are some diseases the symptoms of which simulate clinically those of tuberculosis. I refer particularly to substernal hyperthyroids. These patients may have fever, anemia, exhaustion, loss of weight or rapid pulse and may even have a cough, because of the pressure of an enlarged thyroid against the bronchus. I have known several substernal hyperthyroids and some normally located, only slightly enlarged but hyperactive thyroids, to be treated for tuberculosis over a long period. During the past three years I invited some of the best physicians and surgeons of New York and elsewhere to give lectures to groups of my patients on the subjects in which they specialized. The patients were much impressed with these talks, sitting eagerly through them for three or four hours at a time. Dr. Baehr and some of the other speakers suggested that it would be a good idea to have this method of bringing these talks to the public generally adopted by the members of our profession. The patients demonstrated that they are really eager to learn. It is our task to guide them and teach them the laws of life and the danger signals of disease, to keep them well and to help them recognize and treat their ailments early. I hope that in the near future every physician will realize the value of such educational talks to his own flock.

DR. ESMOND R. LONG, Philadelphia: These papers deal essentially with the underlying mechanism in the pathogenesis of tuberculosis, the early recognition of the disease and its arrest and cure. The early stages of tuberculosis are essentially constructive as far as the nature of tissue substance is concerned. The early tuberculous mass, consisting of cellular collections, even if fundamentally exudative in origin, is solid rather than liquid in character. This means that it is limited in its location and that there is little fluid movement in the bronchi and relatively little absorption of products of death either of tissue or of bacilli. Under such circumstances few symptoms result, and physical signs dependent on exudate or liquefied tissue in the air passages are not present. A patient in this stage is not sick, nor would physical examination in some routine way be likely to bring his trouble to light. However, he is in grave danger. His disease process is analogous to an unfired charge of explosive powder. Should the tuberculous tissue break down, all the elements are at hand for rapid spread. Tubercle bacilli are numerous in softening caseous tissue, and the bronchial channels permit immediate and extensive spread to healthy parts of the lung. With this spread of highly infectious material come cough, fever and the chain of clinical events characteristic of tuberculosis. The onset of the disease is naturally dated by the patient with the onset of these symptoms, yet the true onset antedated this symptomatic outburst by months or even years. Since the task of controlling the first or relatively symptomless stage of tuberculosis is far easier than controlling spread and repair of damage after softening and cavity formation have set in, we must have recourse, as both Dr. Amberson and Dr. Hetherington have pointed out, to methods that detect tuberculosis in its earliest or symptomless stage.

THE ORAL ADMINISTRATION OF PROSTIGMIN IN THE TREATMENT OF MYASTHENIA GRAVIS

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Shortly after the introduction in 1934 of parenterally administered prostigmin in the treatment of myasthenia gravis, prostigmin given orally was also shown to be effective in ameliorating the symptoms of this disease. Administering doses of 30 mg. by mouth three times a day, Everts [1] had encouraging results in two patients after two or three months of treatment. No untoward symptoms were noted. Only a few other reports have appeared: those of Schneider,[2] Laurent and Walker [3] and Smith [4] and a report from our clinic by Mitchell.[5]

It was soon found that 30 mg. of prostigmin by mouth was about as effective as 0.5 mg. given subcutaneously or intramuscularly. The ordinary dose by mouth therefore was from three to six tablets, of 15 mg. each, a day. Laurent and Walker,[3] beginning about June 1935, soon ran out of supplies of prostigmin to be given orally and had to substitute a similar drug known as Substance 36. About 50 mg. of this drug by mouth gave an effect equal to that produced by 1 mg. of parenterally administered prostigmin. In no case did they note unpleasant symptoms or an aggravation of the myasthenic condition of their patients. Smith [4] reported that in one case prostigmin was used orally "with even greater benefit than by injection." Mitchell [5] observed nine patients; his results are incorporated in the present paper. No severe reactions were noted by any of the workers when prostigmin was

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1. Everts, William H.: The Treatment of Myasthenia Gravis by the Oral Administration of Prostigmin, Bull. Neurol. Inst. New York **4**: 523-530 (Dec.) 1935.
2. Schneider, M. Elizabeth: Die Prostigminbehandlung der Myasthenie, Monatschr. f. Psychiat. u. Neurol. **94**: 123-131 (Oct.) 1936.
3. Laurent, L. P. E., and Walker, Mary B.: Oral and Parenteral Administration of Prostigmin and Its Analogues in Myasthenia Gravis, Lancet **1**: 1457-1459 (June 27) 1936.
4. Smith, William A.: The Treatment of Myasthenia Gravis, J. M. A. Georgia **26**: 26-31 (Jan.) 1937.
5. Mitchell, Roger S.: Experience with Oral Prostigmin Therapy in Myasthenia Gravis, New England J. Med. **216**: 96-97 (Jan. 21) 1937.

given orally to patients with myasthenia gravis. Goodman and Bruckner,[6] however, noted severe symptoms due to poisoning when one of them (Goodman), a man in good health, took 45 mg. of prostigmin orally in a single dose. There were vigorous tonic contractions of the muscles of the skeletal and visceral systems, presumably due to the inhibition of the normal esterase at the motor end-plate and the prolonged stimulation by acetylcholine, as noted by McGeorge.[7] Goodman and Bruckner felt that, because of their experience, prostigmin should not be used for the present by mouth. The warning, as far as our observations and those of others [8] are concerned, was unnecessary.

REPORT OF CASES

The eighteen patients whose brief case histories are given hereafter have been taking prostigmin by mouth continuously for from one to fourteen months. Some were known to us years ago; others have come to the clinic only recently. The former patients were treated in the past with aminoacetic acid, ephedrine and other drugs, often with considerable effectiveness. Since the advent of the prostigmin test of Viets and Schwab,[9] the number of patients entering the clinic has greatly increased over former years, fifteen having been added from June 1936 to July 1937. This report covers the period from May 1936, when prostigmin [10] was first administered orally by us, to July 1937.

CASE 1.—J. K. K. (Massachusetts General Hospital), an unemployed man, aged 70, first noticed ptosis of his right eye and diplopia in January 1935. A year later, dysphagia, regurgitation of liquids through his nose and ptosis of the left eyelid occurred, and chewing movements became weak. On a number of occasions he had to be fed by tube, and his condition was considered critical. In prostigmin tests in May and June 1936 he scored 32 and 37 points on the old scale.[9a] Benzedrine and aminoacetic acid were tried without effect; ephedrine gave slight improvement. Prostigmin, given orally since May 1936, has effected a good and continuous remission. Dysphagia and dysarthria are largely controlled; ptosis and diplopia, partly so. The present maintenance dose is 15 mg. of prostigmin taken nine times a day, supplemented with three-eighths grain (0.024 Gm.) of ephedrine three times a day and from 10 to 15 drops of tincture of belladonna three times a day.

CASE 2.—R. S. H. (Massachusetts General Hospital), a salesman, aged 49, first noticed general weakness in the fall of 1935. About January 1936 he could hold up his head for only short intervals and weakness of his arms and legs forced him to give up an office position. Dysphagia and dysarthria, as well as diplopia, came on rapidly, and he entered the hospital in March 1936. His score in the prostigmin test was 68 points. Ephedrine and benzedrine gave partial relief. Oral administration of prostigmin was started in May 1936. The patient has regained some weight, and the dysphagia and dysarthria have in large part disappeared, but the weakness of the neck continues, necessitating support by a Thomas collar. The patient, although not able to work, is greatly improved, having progressed from a critical condition to one in which life is tolerable. He is able to come to the hospital at frequent intervals. His present maintenance dose is as follows: prostigmin, 15 mg. nine times a day; ephedrine, three-eighths grain (0.024 Gm.) three times a day, and tincture of belladonna, 5 drops for each 15 mg. of prostigmin.

CASE 3.—M. G. (Massachusetts General Hospital), a woman, aged 76, noticed bilateral ptosis, dysphagia and weakness in chewing and in using her hand about April 1936. Her symptoms were worse after emotional stress and particularly late in the day. The result of a prostigmin test in June 1936 was reported as 70 points. Oral administration of prostigmin was begun at this time, and the patient reported by letter that she was "much better" in July 1937. Her maintenance dose has not been definitely determined.

CASE 4.—M. J. M. (Massachusetts General Hospital), a truckman, aged 62, first noticed ptosis in February 1934, followed by occasional attacks of diplopia in the next year. Dysphagia and dysarthria, coming on in the spring of 1935, led him to enter the hospital in July 1936. The score of his prostigmin test was 58 points. Unable to speak or swallow, he was first treated by intramuscular administration of prostigmin. Within an hour he could take 15 mg. of prostigmin by mouth. During the next four months he improved only slightly with an irregular consumption of six tablets a day, with belladonna. Marked dysphagia and dyspnea developed, and he entered the hospital in October 1936, moribund. He was quickly revived again by intramuscular injection of prostigmin, and his oral dose of prostigmin was increased to eight tablets a day, with potassium chloride. In January 1937 his condition was good; he drove his automobile and had gained 25 pounds (11 Kg.).

In the middle of February 1937 the patient had a cold and shortly afterward some difficulty in swallowing his prostigmin tablets. Three or four days after the onset his condition became decidedly worse. He entered the hospital February 22, showing marked dysphagia and dyspnea. Prostigmin, 4.5 mg., injected intramuscularly, gave him considerable relief, but the effect of this drug did not continue, and on February 24 he died, showing respiratory embarrassment and elevation of temperature. There were no signs of pneumonia. No postmortem examination was allowed.

CASE 5.—J. B. (Massachusetts General Hospital), an unemployed man, aged 20, was first seen in May 1932 with generalized muscular weakness of ten months' duration, associated with dyspnea, dysphagia and diplopia. He took ephedrine from 1932 to 1935, with moderate effect. Aminoacetic acid was used in 1935, with less effect than ephedrine. His condition became much worse, over a period of a few months, when he stopped taking both drugs. Injections of prostigmin in April 1935 caused marked improvement, and he continued taking two ampules, intramuscularly, a day until July 1936, when he changed to prostigmin by mouth. In his prostigmin test he scored 47 and 60 points on two occasions. Six tablets of prostigmin, 15 mg. each, did not control his symptoms, and it was found that his maintenance dose had to be raised to twelve tablets a day, with three-eighths grain of ephedrine three times a day and 3 drops of tincture of belladonna three times a day. Taking this dose he is able to come to the clinic each month but is not able to work. He has no dysphagia or diplopia.

CASE 6.—E. H. (Massachusetts General Hospital), a housewife, aged 27, had dysarthria, diplopia and dysphagia for four or five months before entering the hospital in March 1932. She responded slightly to ephedrine, and at times all the symptoms except the diplopia were nearly absent. During pregnancy she was much improved. She had a relapse three months after delivery. Seen again in August 1936, she had all her previous symptoms. In her prostigmin test she scored 45 points. Oral administration of prostigmin was begun in August 1936. Her maintenance dose is as follows: prostigmin, 15 mg., ten tablets a day, with tincture of belladonna, from 3 to 5 drops three times a day. Her condition is good.

CASE 7.—F. J. R. (Massachusetts General Hospital), a salesman, aged 66, had dysarthria in 1932, lasting a week. In 1934 his condition became acute, with weakness of the muscles of the neck, dysphagia, dysarthria, regurgitation of fluid through his nose and diplopia. In November 1934, while in the hospital, he began taking ephedrine and aminoacetic acid, with slight improvement. On four occasions he took physostigmine sulfate without effect. Potassium chloride and prephysin (Chappel) were also tried; the patient grew worse and returned to ephedrine and aminoacetic acid. In his prostigmin test he scored 49 points. In August 1936 he began taking prostigmin by mouth. His maintenance dose in July 1937 was as follows: prostigmin, 15 mg. twelve times a day, with atropine sulfate,

6. Goodman, Louis S., and Bruckner, William J.: The Therapeutics of Prostigmin: A Warning Concerning Its Oral Use Based on a Personal Experience, J. A. M. A. **108**: 965-968 (March 20) 1937.
7. McGeorge, Murray: Choline Esterase Activity in Disease with Special Reference to Myasthenia Gravis, Lancet **1**: 69-72 (Jan. 9) 1937.
8. Thorner, Melvin W.: The Therapeutics of Prostigmin, J. A. M. A. **108**: 1449-1450 (April 24) 1937.
9. (a) Viets, H. R., and Schwab, R. S.: Prostigmin in the Diagnosis of Myasthenia Gravis, New England J. Med. **213**: 1280-1283 (Dec. 26) 1935. (b) Viets, H. R., and Mitchell, R. S.: The Prostigmin Test in Myasthenia Gravis: Second Report, ibid. **215**: 1064-1065 (Dec. 2) 1936.
10. Part of the drug was supplied by Hoffmann-La Roche, Inc. Funds for this study were donated by the F. E. Weber Charities, Boston.

1/200 grain (0.3 mg.) four times a day. At present he is able to walk, talk and swallow without difficulty. There is no diplopia. His general condition is good, but he could not return to his former occupation.

CASE 8.—M. T. (Dr. E. M. Cole), a woman, aged 53, a bookkeeper, first complained of general weakness and diplopia about January 1936. Her symptoms increased rapidly in July 1936, so that she could not lift her head from the bed. There were dysarthria, dysphagia and ptosis. All her symptoms grew more pronounced toward evening. In her prostigmin test she scored 68 points. Her maintenance dose is 15 mg. of prostigmin six times a day and from 5 to 10 drops of tincture of belladonna three times a day.

CASE 9.—F. G. (Dr. J. B. Ayer), a housewife, aged 37, began to have the symptoms of ptosis, diplopia and general muscular weakness in 1923. Dysarthria was an added symptom in 1928. At this time she could not turn over in bed. With ephedrine and aminoacetic acid she improved in 1930. In her prostigmin test in 1936 she scored 52 points. She began taking prostigmin by mouth in August 1936, with better results than with any previous form of medication. Her maintenance dose in July 1937 is from six to eight tablets a day. Her condition, in spite of her long illness, is good.

CASE 10.—M. H. (Massachusetts General Hospital), a woman aged 23, a student, acquired ptosis and diplopia about 1930. A year later the trunk and the extremities were involved. In 1932, during a relapse, she was confined to bed and had difficulty in swallowing. For about five years she has been taking ephedrine, with partial relief. She is worse during her catamenia. In her prostigmin test she scored 35 points. Her maintenance dose at present is prostigmin 15 mg. eight times a day, with ephedrine, three-eighths grain, four times a day. She is very well, free from symptoms and able to work.

CASE 11.—F. E. S. (Palmer Memorial Hospital), a man aged 59, a physician, first noticed diplopia in 1932. It lasted a month, and no other symptoms appeared until June 1936, when dysphagia developed, followed by dysarthria, ptosis and mental depression. In his prostigmin test he scored 39 points in September 1936. He began taking prostigmin by mouth at that time. His maintenance dose is five or six pills a day and ephedrine, three-eighths grain three times a day. Totally incapacitated at the time of admission to the hospital, he is now able to see a limited number of patients and drive his automobile.

CASE 12.—J. L. P. (Massachusetts General Hospital), a fireman, aged 52, first noticed ptosis and diplopia in December 1936. His symptoms were worse in the afternoon. There was no dysarthria or dysphagia and no general weakness. The result of his prostigmin test, with the revised score, was 46 points. The administration of prostigmin by mouth was begun in February 1937. His maintenance dose is eight pills a day, with atropine sulfate, 1/50 grain (0.4 mg.) three times a day. He is now able to work.

CASE 13.—F. D. (Massachusetts General Hospital), a millworker, aged 50, first noticed ptosis and diplopia in April 1936. He was worse in the afternoon. In his prostigmin test he scored 58 points. He began taking prostigmin by mouth in March 1937, and his maintenance dose in July was nine pills a day, with ephedrine, three-eighths grain two times a day.

CASE 14.—S. J. S. (Massachusetts General Hospital), a housewife, aged 47, first had ptosis in 1933, with weakness of her neck. In 1936 there was weakness of her arms. Electromyograms and ergograms showed myasthenia gravis. Oral administration of prostigmin was begun in April 1937. Her maintenance dose is eight pills a day. She is moderately improved.

CASE 15.—S. S. (Massachusetts General Hospital), a housewife, aged 62, had ptosis in 1928 for two months. It occurred again in the fall of 1936. Diplopia developed within a few months, and both symptoms were worse in the afternoon. The result of her prostigmin test, with the adjusted score, was 35 points. Improvement was noted with a maintenance dose of six pills a day.

CASE 16.—L. P. R. (Massachusetts General Hospital), a housewife, aged 22, began to have dysphagia in April 1937, with general weakness and dysarthria in the afternoon. Some ptosis was noted in June 1937. The result of her prostigmin test, with the revised score, was 50 points. Her initial dose was four tablets of prostigmin a day.

CASE 17.—M. K. (Massachusetts General Hospital), a schoolgirl, aged 14, began to have dysarthria, dysphagia and general weakness in the summer of 1935. In her prostigmin test she scored 49 points. Some improvement was noted while she was taking ephedrine. She began taking prostigmin by mouth in July 1937, her initial dose being four pills a day.

CASE 18.—N. G. (Massachusetts General Hospital), a housewife, aged 46, first noticed diplopia in October 1934. Because of her hypertension the condition was thought to be due to cerebral hemorrhage. Ptosis developed in 1935. Her prostigmin test showed myasthenia gravis. Her initial dose of prostigmin was four tablets a day.

In the month of July three additional patients were seen in the clinic. They are doing well on prostigmin taken orally.

COMMENT

Dosage.—Prostigmin is supplied in tablets of 15 mg. each for oral administration. Our doses have been from four to twelve tablets a day. The initial dose is spaced at four hour intervals, usually four tablets a day. This dose is often too small to maintain muscular efficiency, and it must be increased to from six to twelve tablets in the twenty-four hour period. A maintenance dose, established in two or three weeks,

Name: J. K. K. Unit # 6329 Date: 8/17/37

	A.M.				P.M.										10 P.M.
	8	9½	10	11	12	1	2	3	4	5	6	7	8	9	10 to 6 A.M.
Medicine															
Pills															
Prostigmin	..	1	..	..	2	..	..	1	..	..	2	..	..	..	1	2
Drops															
Tr. Belladonna	..	..	..	..	8	..	..	..	..	..	8	..	..	..	..	8
Ephedrine	..	..	..	..	⅜	..	..	..	..	..	⅜	..	..	..	..	⅜

Dosage chart used in case 1.

will average from four to nine tablets a day. This dose in thirteen of our cases is as follows: two cases, twelve tablets a day; one case, ten; three cases, nine; three cases, eight; one case, from six to eight; three cases, six. These doses have been maintained with slight variation from two to fourteen months: three cases, fourteen months; one case, thirteen; two cases, eleven; one case, ten; two cases, five; four cases, four; two cases, three.

For patients taking prostigmin by mouth, the spacing of the doses has been of considerable aid in maintaining muscular efficiency during the waking hours. With six tablets a day, the doses are taken at 6 and 9 a. m., 12 noon, and 3, 6 and 9 p. m. The dose may be doubled before meals, at 6 a. m., 12 noon and 6 p. m., making an intake of nine tablets, or 135 mg. of prostigmin, a day for an adult. This, according to our experience, is the common maintenance dose for a severe case of myasthenia gravis. A few patients require two tablets at each of the six periods, or twelve tablets a day. This dose has been taken by two of our patients (cases 5 and 7) for ten or twelve months. Unequal spacing in some cases may give the best results. In view of this fact we use a printed chart showing the hours from 8 a. m. to 10 p. m. in columns, with another column for the night. The drugs used are written in, and the chart is given to the patient, showing the time when the drugs are to be taken.

Effect.—Thirty milligrams of prostigmin administered orally is, in most instances, equivalent to 0.5 mg. of

prostigmin in a 1 : 2,000 solution given intramuscularly. The effect, however, is not so prompt and is less likely to be complete. The response comes in about one-half hour, reaches a maximum in one or two hours and wears off in three or four hours. During this period the paretic muscles regain their power in part or in whole. The visceral disturbances are variable. Some patients have none; others complain of considerable abdominal discomfort, diarrhea or a desire to evacuate the bowels. When disagreeable symptoms are induced by prostigmin given orally they may be controlled by tincture of belladonna in doses of from 3 to 15 drops or by atropine sulfate, 1/200 grain (0.3 mg.) given with the prostigmin. Twelve of our eighteen patients took belladonna or atropine, the dose varying in amount with the abdominal discomfort. The visceral symptoms are often absent when only one tablet of prostigmin is taken at a time.

Patients with severe myasthenia gravis often have great difficulty in getting out of bed in the morning when the effect of the prostigmin taken the night before has worn off. A few patients have been wakened at 1 or 2 a. m. to take one or two tablets. Most of them take two tablets as soon as they wake up, either by themselves or with aid. For those who have difficulty in swallowing early in the morning, prostigmin is now being tried in suppository form. In the most severe cases an ampule of prostigmin should be at hand for emergency injection.

Adjuvant Drugs.—In the last year many of the drugs used in the treatment of myasthenia gravis before the days of prostigmin have been experimented with as adjuncts to prostigmin. Those still in use by our patients are potassium chloride, ephedrine and benzedrine. A few patients think potassium chloride valuable in prolonging and "evening out" the effects of prostigmin. The drug, however, is gradually being given up. When three-eighths grain of ephedrine was added to the prostigmin, more than one half of our patients were improved. With it the patients have less abdominal discomfort, and often the amount of prostigmin can be reduced when ephedrine is taken.

CONCLUSIONS

Oral administration of prostigmin may be safely used in the treatment of patients with myasthenia gravis in daily doses of from three to twelve tablets of 15 mg. each. When ingestion of the drug is carefully spaced, patients maintain a reasonable degree of muscular efficiency, certainly better than with any other form of treatment. No ill effects were noted in eighteen patients treated from one to fourteen months. Other drugs may be added to the prostigmin regimen with benefit.

ADDITIONAL NOTE

Since this paper was written, during the months of July, August and September, five new cases were added to the clinic:

CASE 19.—E. A. (Massachusetts General Hospital), a housewife, aged 21, first noticed dysphagia in 1934; ptosis occurred in 1936. Her prostigmin test score was 32. Beginning with an initial dose of four tablets of prostigmin a day, she is now taking six tablets with symptomatic relief.

CASE 20.—E. T. (Massachusetts General Hospital), a schoolgirl, aged 17, has suffered from ptosis, diplopia and ophthalmoplegia since 1933. Her prostigmin test was scored at 55 points. Under a dosage of four tablets a day, with one occasionally in the evening, the patient is partly relieved of her symptoms.

CASE 21.—T. E. (Massachusetts General Hospital), a man, aged 53, first noticed ptosis and partial ophthalmoplegia in the spring of 1937. His prostigmin test score was only 16. On four tablets a day there has been well marked improvement.

CASE 22.—B. R. (Massachusetts General Hospital), a man, aged 48, first noticed diplopia and ptosis of the left eye eleven months before admission. He complained, however, of weakness in his neck and arms practically all his life. His prostigmin test score was 45. On five tablets a day there has been distinct improvement.

CASE 23.—L. B. (Massachusetts General Hospital), a housewife, aged 66, first noticed weakness of her legs two or three years before admission. For about eight months she had had ptosis of both eyelids. Prostigmin given subcutaneously gave prompt relief of the ptosis. A dosage of from three to four tablets a day has resulted in partial symptomatic relief.

During the last three months, attempts have been made to reduce the amount of prostigmin and the adjuvant drugs. In one case the prostigmin was reduced from eight to five tablets a day and in three others a reduction of one or two tablets has been made without ill effects. In practically all the cases, moreover, atropine has been omitted and belladonna reduced to from four to eight drops, three times a day. Only one of our patients is now taking potassium chloride.

THE TREATMENT OF NEPHROSIS IN THE YOUNG CHILD

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AND
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The treatment of nephrosis, the chronic renal disorder so peculiarly prevalent in childhood and adolescence and of which the exact etiology it still quite obscure, offers many perplexing problems to the practitioner.

Aside from its chronicity, one of the most disconcerting characteristics is its tendency to alternate remission and severe exacerbation and its reappearance after long periods of apparent cure.

Although considerable progress has been made in the treatment of the condition, no form of therapy is really consistently successful or gives assured relief for the more troublesome symptoms. Outstanding among these and most alarming are the excessive, sometimes huge, losses of protein in the urine and the development of anasarca and ascites to a degree hardly equaled by any other condition affecting the child.

The albuminuria cannot be treated but can be overtreated, much to the harm of the patient when it is made the excuse for excessive limitation of the protein intake. Considerable changes in the protein content of the diet have little or no effect on the daily proteinuria. In this condition there is no need to worry about nitrogen retention in the blood on ordinary or even moderately elevated protein diets.

The edema in the nephrotic child is usually the special object of therapy and relief from it the chief concern. Rest in bed is always absolutely essential. Practically all hydrotherapeutic measures are feeble agents for the relief of edema.

Restriction of salt and fluid intake is of the greatest importance, will always affect the condition favorably and may give temporary or complete relief even though edema favoring factors such as persistent albuminuria

From the Department of Pediatrics, University of Chicago Clinics.
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and low plasma proteins may still be present or persist. Common sense and the general state of the patient must guide the rigidity of this restriction.

The fairly well nourished child, even with some edema, is better off than the child made edema free at the expense of gross emaciation. Excessive restriction of water in the young child may effect great hardship and is not without danger from the development of toxic states.

Practically all forms of diuretics, such as the purines, theobromine, the acid-forming diuretics and the mercurials, are entirely or relatively safe because the functional capacity and structure of the kidney are not essentially damaged; but their effect in nearly every instance is quite disappointing and practically never of sustained value.

Thorough removal of focal infections, especially about the upper respiratory tract, a procedure particularly emphasized and championed by our late lamented colleague Marriott and his associates, often is truly spectacular in its effect, but again it will completely fail in case after case. Our experience with repeated blood transfusions has not been very striking.

Mechanical removal of excessive edema fluid often becomes imperative and will frequently have a very favorable effect on the whole condition and especially the reestablishment of an active diuresis.

All these procedures must be done with great care and under the strictest asepsis. I recall three cases in which a continual siphonage of ascitic fluid from the abdomen for a period of from three to four weeks effected a complete cure. A fourth patient died of pneumococcic peritonitis.

A few years ago A. Osman of London published some results on the treatment of acute and chronic forms of nephritis with high doses of alkali. It was advocated particularly for cases in which generalized anasarca and ascites were predominant features. Additional favorable reports appeared subsequently in *Guy's Hospital Reports* and the *Lancet*.

Osman and many others before him have found that some degree of acidosis is practically the rule in both acute and chronic renal disease. It has been quite definitely established that the accumulation of phosphate is probably the principal factor in the production of this acidosis. Not alone does there seem to be a decrease in the plasma bicarbonate in cases of nephritis, but there seems also to be an increase in alkali tolerance. There seems to be no direct relationship between the degree of acidosis as measured by the plasma bicarbonate and the severity of the symptoms present.

The procedure of high alkali therapy in renal disease is based primarily on some theories expressed by Martin Fischer over a decade ago, who held that the colloidal proteins of the body tissues and cells have the property of imbibing or parting with water with alterations in the surrounding medium. Any change in the acid-base relationships, such as alteration in the reaction of the medium and change from the iso-electric point, results in significant change in cellular water content and its distribution in the body. While the theories of Fischer have been criticized and are still controversial, there are some aspects of them which offer reasonable explanations of this peculiar action and the effect of alkalis in the treatment of some renal disorders.

It is more than probable that many of the biochemical disturbances found in the blood in nephritic patients are determined in part at least by the permeability or physical condition of the membrane of the renal cells. It is probably here that the explanation of the effect of alkalis in chronic renal disease must be sought. It is on the basis of some of these theories and concepts that Osman suggests his procedure. He believes that alkalis may be used with advantage in many cases of nephritis under certain circumstances for either their prophylactic or their therapeutic value.

Summary of Fourteen Cases of Nephrosis

Case	Sex	Age, Yrs.	Type	Probable Duration	Chief Symptoms	Maximum Blood Urea, Mg. %	Maximum Diuresis, Oz. per Day	Total Weight Loss, Pounds	Effect on Edema	Comment
1	♂	3	Chronic parenchymatous	1 yr.	Anasarca, ascites	..	70	10½	Cleared entirely	No edema or albumin; well 1 yr. later
2	♂	2	Chronic parenchymatous	1 yr.	Anasarca, ascites	..	..	3¾	Cleared	No edema or albumin; died from summer diarrhea later after recovery
3	♂	3	Acute parenchymatous	1 mo.	Extreme anasarca and ascites	..	..	....	.....	Edema and albumin cleared but patient died of pneumococcic peritonitis; kidneys at autopsy normal
4	♀	4½	Chronic parenchymatous	6 mos.	Anasarca, ascites	67	61	18	Cleared entirely	Edema cleared up but returned and then not controlled; died; no autopsy
5	♂	2½	Acute parenchymatous	3 mos.	Anasarca, anuria, no ascites	..	..	....	Cleared	Treatment omitted at home; readmitted 1 mo. later; anasarca, anuria, ascites; died
6	♀	4	Chronic parenchymatous	3 mos.	Anasarca, ascites; traces of blood in urine	12	..	....	.....	No result from treatment; continued to do badly and died; no autopsy
7	♀	5	Chronic parenchymatous	2 yrs.	Anasarca, ascites	32	75	....	Cleared entirely	Relapsed 6 times in 4 yrs., cleared up each time with treatment
8	♀	9	Chronic parenchymatous	11 mos.	Anasarca, ascites	..	..	....	Cleared	Edema cleared but patient died of pneumococcic peritonitis
9	♂	6	Chronic parenchymatous	6 mos.	Extreme anasarca, ascites	44	44	11½	Cleared entirely	No further treatment; well 5 yrs. later
10	♂	13½	Chronic mixed symptoms	10 yrs.	Edema of face, legs; slight ascites	39	87	6	Cleared	No edema for 4 yrs.; most of albumin cleared; blood urea increasing; improved
11	♂	7	Chronic parenchymatous	8 mos.	Anasarca, ascites	29	60	....	.....	Remained free from edema for 4 yrs. under treatment, then died of pneumococcic peritonitis
12	♂	5½	Acute parenchymatous	? wks.	Anasarca, ascites	..	..	....	.....	No result from treatment; died from tetany
13	♀	4	Chronic parenchymatous	1 yr.	Anasarca	..	60	9	Cleared entirely	Well
14	♂	7	Chronic parenchymatous	1 yr.	Anasarca, ascites	..	..	....	Cleared entirely	Edema returned twice and twice cleared up with treatment

Results: Died, 8; improved, 1; well, 5

It is important to know the plasma bicarbonate level before treating a case of nephritis with alkalis.

Cases of nephritis presenting edema, high albuminuria and low urinary volume are likely to derive the greatest benefit from alkalis given in amounts sufficient to raise the plasma bicarbonate to a normal level and maintain it at that point. In favorable cases a marked diuresis and subsidence of edema will occur when this point is reached. The output of albumin is generally greatly diminished, and it may in time completely disappear.

The acute or chronic parenchymatous or nephrosis type of renal disease with little or no structural impairment of the kidneys offers the most suitable case for this form of treatment. Also, however, it is useful in the treatment of mixed forms in which there is considerable structural damage and oliguria and edema with low plasma bicarbonate level. It is least effective in the chronic interstitial forms with hypertension, although even in these cases it may give some relief for excessive edema if the plasma bicarbonate level can be raised.

While this form of treatment in no way restores a structurally damaged kidney or stays a process operating to that end, one can expect with certain confidence a marked improvement or even complete regression of some of the distressing symptoms of the case, such as excessive edema, oliguria, anuria or excessive proteinuria, provided enough alkali is given to restore the plasma bicarbonate to a normal level and to keep it there.

The treatment often calls for truly heroic doses of alkali and is not altogether without danger. Overdosage must be guarded against by a periodic checking of the plasma bicarbonate. The alkaline salts are given by mouth until the plasma bicarbonate reaches a normal value, or in the absence of untoward symptoms they may be given even beyond this point. Confinement to bed is essential except in the mildest case, and the treatment is best carried out under hospital management.

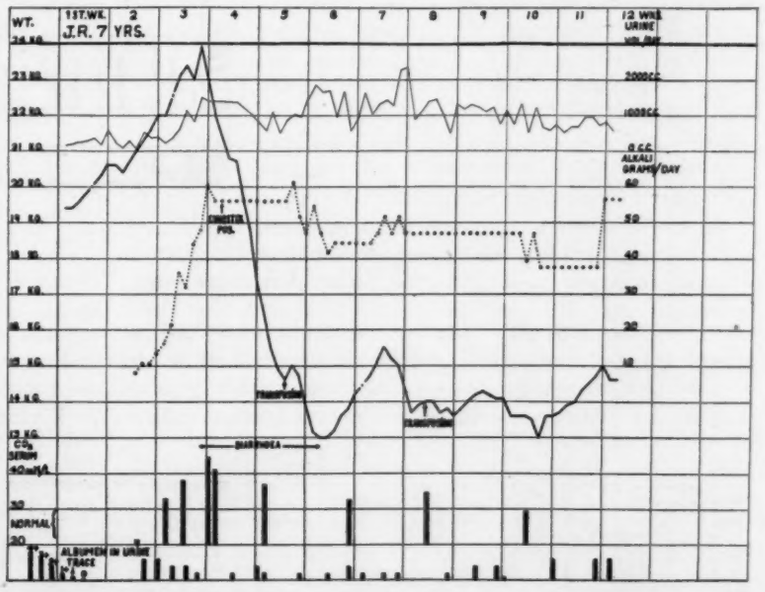

Chart 1.—Patient made complete recovery. Note marked diuresis at maximum intake of alkali.

Except in the presence of oliguria or hematuria, an ordinary mixed diet without restriction of protein or salt can be allowed. No excessive restriction of fluid need be imposed, although care must be taken that the fluid intake does not greatly exceed the fluid output.

The alkalis are given in the form of potassium citrate, potassium bicarbonate, sodium citrate and sodium bicarbonate, generally in equal quantities. Water is added and some flavoring agent, enough to disguise the taste. Syrup of orange or peppermint water and chloroform water are good agents.

The potassium salts are more effective in reducing edema and promoting diuresis than are the sodium salts, but the former are more dangerous on account of possible toxic action on the heart. The sodium salts, though less powerful, have much the same action. If used alone they cause more initial increase of edema than if used in combination with the potassium salts.

All the salts may cause some unfavorable effects; the bicarbonates tend to cause nausea and vomiting and the citrates often produce alarming diarrhea, especially in children. All these difficulties are best overcome by combining the salts as described. In cases of coma, the alkalis may be given by rectum as a 3 per cent solution of the foregoing mixture. Intravenous therapy with the alkalis has been attempted but is not very successful and is technically difficult. During the treatment the total amount of urine passed in the twenty-four hours must be known, a record of the patient's weight must be kept and the reaction of the urine must be tested on early morning specimens.

The plasma bicarbonate should be estimated before the treatment is started and again at intervals during the treatment, especially if untoward symptoms supervene. For children the initial dose of the four alkalis in equal mixture is from 2 to 3 Gm. or 30 to 50 grains three times a day. The following day this amount is given four times a day, or a total of from 8 to 12 Gm. or 120 to 200 grains. Thereafter the dose is increased by 2 or 3 Gm. a day until the p_H of the urine is from 7 to 7.6. Dosages of from 30 to 40 Gm. or 500 to 800 grains a day, and even higher, may be reached with safety. The weight generally increases markedly at first and an extremely marked, even alarming, initial increase of the edema is practically a constant feature in all cases. Estimation of plasma bicarbonate at frequent intervals is necessary at this stage. In spite of the marked increase of the edema, it is necessary at this point to increase the dosage of alkali fearlessly until the plasma bicarbonate reaches a normal level or beyond and to keep the dosage continually high for some time, unless symptoms of toxic alkalosis, such as tetany, heart weakness or excessive diarrhea or vomiting, make a diminution of the dose especially of the potassium salts imperative. A remarkable diuresis usually sets in shortly after the height of the dosage has been reached; the p_H of the urine is between 7.6 and 8.3 and the plasma bicarbonate is at normal level or above. This diuresis usually continues and often in an amazingly brief time causes complete loss of edema, marked diminution or complete disappearance of albumin from the urine and great reduction in lipemia.

Three dangerous symptoms must be looked for and guarded against at this stage of the case. Tetany and even convulsive seizures may develop. Symptoms of dangerous heart weakness may appear or excessive vomiting and diarrhea may develop. Tetany can be

prevented or usually relieved by the repeated intramuscular use of calcium chloride in a dosage of 0.05 Gm. For the heart weakness and excessive diarrhea a diminution of the alkali, particularly the potassium salts, is advisable and often imperative. It is seldom necessary to reduce the dose by more than one third of the maximum amount, and it is often sufficient to reduce only the potassium salts. We have found it necessary to reduce these sharply in the face of dangerous symptoms.

Even in the face of threatening dangers, the success of the treatment depends on a bold and fearlessly continued use of relatively high doses of alkali. When active diuresis has set in, it is unnecessary to increase the alkali further, but the high dosage must be maintained at all costs until the edema has entirely disappeared and the volume of urine has gradually fallen to normal. It may take from ten days to several weeks before this is accomplished, but the dose must not be reduced before this stage is reached. Any reduction commonly leads to a return of the edema, albuminuria, oliguria and even complete anuria. The latter condition is liable to occur if all alkali is withdrawn rapidly or completely.

After the urinary volume has returned to normal, a gradual reduction of the dose may be effected. Any return of the symptoms must be met at once by a resumption for at least a few days of the maximum dose. A substantial dose of alkali should be continued for a considerable period after all edema has disappeared and the urine has cleared entirely of albumin, in order to insure against return of active symptoms.

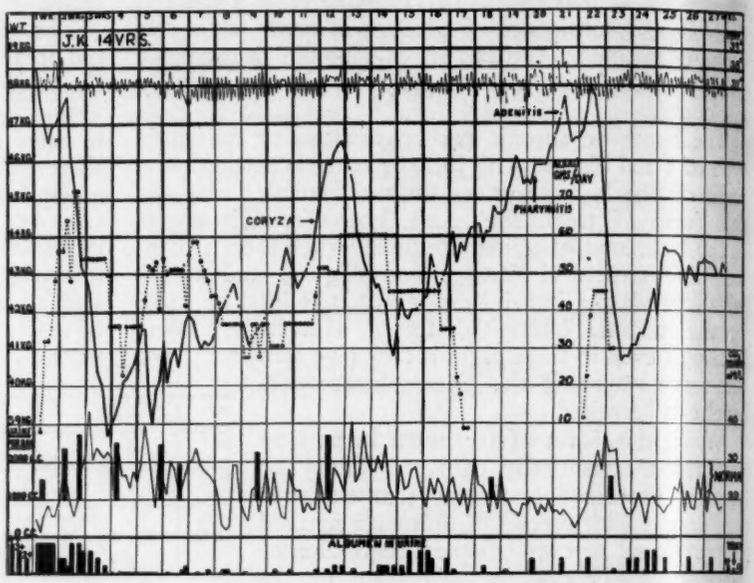

Chart 3.—Patient eventually completely recovered but shows the relapses due to severe intercurrent infections.

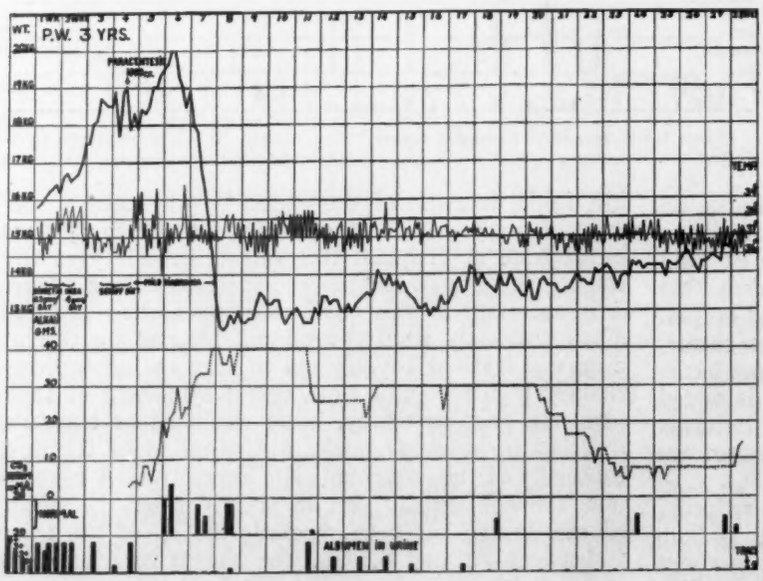

Chart 2.—Patient had apparently made complete recovery but eventually succumbed to an acute hemolytic streptococcus infection.

Estimation of the plasma bicarbonate is probably the best check on favorable or unfavorable response to the treatment. It is commonly found that, if treatment is omitted or improperly managed before the "cure" is complete, a much larger dose is required in a second attempt to secure the same result, if it can be obtained at all.

The high alkali treatment will not relieve every case of nephrosis, but it will almost certainly relieve the troublesome edema and reduce or stop the proteinuria. It cannot prevent or significantly modify the serious complications such as pneumococcic or streptococcic pneumonia or peritonitis or cellulitis, but there is no doubt that the removal of edema fluid from the tissues must afford a considerable measure of protection against the development of these infections.

In a series of forty cases reported by Osman, thirteen patients with nephrosis ranged in age from 2 to 7 years; one with a mixed form of the disease was over 13 years. In nearly all the cases the disorder had existed from six months to over a year and was characterized by excessive anasarca and ascites. Of the fourteen cases, five were completely cured, one was permanently improved and eight were fatal. Three of the deaths were due to pneumococcic peritonitis; one patient died from tetany and one from intercurrent summer diarrhea after recovery from the renal disorder. Two died from relapses after initial success with the treatment and one died without showing any response whatever to the treatment.

Our series at the Bobs Roberts Hospital comprises seven cases. Of these, three of the patients have apparently completely recovered except that in two of the cases any moderately severe infection of the upper respiratory tract, especially acute sinusitis, is followed by a slight transitory return of the edema. Two of the patients have been free from all symptoms for a period of more than three years.

Of the four cases which were fatal, only two were really true cases of nephrosis as shown by autopsy. Two were of the mixed form, showing extensive renal damage. All of them had shown considerable edema before admission to the hospital. Two patients died of pneumococcic peritonitis which developed shortly after their admission to the hospital and before the high alkaline treatment had been well started, although in one of the cases marked diuresis had set in. The

third child died from heart failure within forty-eight hours after admission to the hospital and before effective therapy could be started. The fourth patient, one with true nephrosis, had responded remarkably and repeatedly to the treatment and had apparently completely recovered when a hemolytic streptococcus throat infection suddenly developed, followed by pneumonia and general peritonitis; death occurred within a week after the onset of the illness. Autopsy was refused.

Except for the prompt treatment of minor infections and reasonable supervision of the diet, no particular management seems to be necessary once the patient has recovered.

The favorable experience that we have had in the few cases in which this form of treatment could successfully be inaugurated and followed seems to confirm the favorable results reported by Osman and led us to believe that the use of the high administration of alkalis is probably one of the best forms of therapy available for the treatment of chronic nephrosis and the relief of some of its most troublesome symptoms and should be attempted in all cases that do not readily yield to less drastic measures.

ABSTRACT OF DISCUSSION

DR. A. GRAEME MITCHELL, Cincinnati: One of the most important considerations is to determine whether the patient has what the authors referred to as pure nephrosis. I believe there is such a condition although I think it is difficult to diagnose, and often it can be distinguished from nephritis only after long observation. I have always been discouraged with the treatment of nephrosis. It has given me a feeling of futility. In Cincinnati my colleagues and I have made a definite attempt to try to find out something about it. Over a period of some years we have kept in the metabolism ward several patients suffering from what we originally thought was nephrosis. We discovered later that in some instances the patients had a true nephritis. The most important fact that I discovered was how much it costs to run a metabolism ward. Secondly, we came to the conclusion that we really knew little about what to do for the patient with nephrosis. Theoretically, the condition has bothered me tremendously. The arguments that have led to acid therapy and, on the contrary, to alkali therapy have never been entirely clear to me. Practically, I have sometimes felt that a patient who did not respond to acid therapy would sometimes respond later to alkali therapy or that the reverse of this might happen. After considerable observation I came to the conclusion that the patient did his tricks of retention or loss of fluid on the same regimen and that what I was doing had no particular effect, so that in my innocence I felt that I was doing rather little to help. It is obvious that the authors have been more courageous and more persistent in alkali therapy than I have been and perhaps that is the reason they have obtained results. The danger of alkali therapy should be stressed. I have reached the point where I feel that alkali should never be given unless one has the opportunity to observe the patient under controlled conditions. Close clinical observation is not enough since it is difficult, if not impossible, at times, to distinguish alkalosis from acidosis. Alkali therapy, then, should be carried out only when one has the opportunity to determine frequently the carbon dioxide content of the patient's blood. I have had in the last year four infants with alkalosis on the basis of alkali therapy. Three of these patients died.

DR. FREDERIC W. SCHLUTZ, Chicago: I quite agree with Dr. Mitchell that it is difficult to tell whether one is dealing with a case of true nephrosis or some other form of nephritis. The clinical picture largely must guide one. No claim is made that the alkali therapy will benefit every form of nephritis. It has been the experience, however, of Osman and also our own that it will benefit any case of nephrosis or nephritis in which there is a great deal of edema and proteinuria. These two symptoms are always markedly benefited by the treatment, and particularly so in the nephrosis case. Every one who uses the treatment will be startled by the rapid increase of edema above the amount at the start of the treatment. It seems as though one is doing the patient more harm. It is most important to remember that one must fearlessly increase the salt intake and certainly persist in the use of large amounts in the face of this increase. Only decrease the salts when dangerous symptoms supervene. These are marked diarrhea, evidence of cardiac weakness and major manifestations of tetany. A moderate showing of tetany need give no alarm. It is the potassium salt that must first be reduced and sometimes the only salt that needs to be reduced. It is always necessary to check the plasma bicarbonate when using this treatment. If the plasma bicarbonate approaches normal or slightly above normal levels, the treatment is usually adequate and favorable symptoms will develop. Unless toxic symptoms supervene, the salt mixture can be fearlessly increased until the plasma bicarbonate level approaches normal. This form of treatment should not be carried out in any case of nephrosis or nephritis unless the plasma bicarbonate can be checked at frequent intervals.

MUCOSAL PATTERN TECHNIC AND KYMOGRAPHIC RECORDS OF THE ESOPHAGUS AND STOMACH

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Two newer methods of roentgen technic, useful in gastro-intestinal diagnosis, have enjoyed extensive exposure in the literature of roentgenology and on programs of roentgen societies. It is proposed to expose these methods to the members of the general profession and, at the same time, to inquire critically into their values.

The mucosal pattern, the relief picture or the compression technic of the mucous lining of the gastro-intestinal tract is secured by fluoroscope or roentgenogram after manipulation and gravity have adapted a thin, mucilaginous, opaque medium to the mucosal folds of the esophagus, stomach or small or large intestine. It is a study of the intimate morphologic detail of the mucosa. The regular, bulkier barium sulfate meal provides the diagnostic factors of contour and function and will provide conclusive diagnostic facts in a major portion of appropriate cases. The mucosal pattern technic amplifies the routine examination in certain details of the actual ulcer and cancer or characteristic diagnostic patterns, such as esophageal varices or chronic gastritis.

There are inherent dangers to the roentgenologist in the mucosal pattern technic because of the prolonged exposure of the fluoroscopic studies which may be necessary to secure or identify the favorable filling or pattern which he wishes to record permanently by the roentgenogram. Sometimes this danger is greatly increased among physicians who complete their own roentgen examinations, because they fail to impose on themselves the requirements of eye accommodation, because they do not have the apparatus that roentgenologists know is essential for success with this method and, more pertinently, because they lack a studied familiarity and experience with normal and abnormal mucosal patterns.

Special apparatus is required (1) so that the favorable mucosal pattern can be achieved by compression, position and posture and (2) so that the small, aimed roentgenograms are secured at the right instant. It must be possible to switch from fluoroscopic image to proper radiographic technic instantly. The expense of

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this technical requirement seems to preclude the adoption of this technic by others than roentgenologists.

There are, however, two particular situations in gastro-intestinal diagnosis in which the mucosal pattern technic can be useful without special apparatus or extensive roentgen education. The vagaries of actual and artificial pattern fillings throughout the gastro-intestinal canal are such as to impose great responsibilities of study of and experience with normal and abnormal mucosal patterns on every physician who would pursue these examinations. Undoubtedly the method may be reserved to the skilful roentgenologist and to the gastro-enterologist whose mental and mechanical equipment for roentgen diagnosis rank with those of the qualified roentgenologist.

These two situations of practical and easy application of pattern technic involve (1) the lower end of the esophagus and (2) the general mucosal pattern of the stomach.

Esophageal varices produce a characteristic shadow of uneven, tortuous mucous membrane. The normal esophageal mucosa shows long, thin, evenly spaced lines running parallel throughout this lengthy tube. The ordinary heavy barium sulfate meal masks both the normal and the abnormal mucosal pattern. Any thin, mucilaginous opaque mixture swallowed by the patient while in a favorable, prone, esophageal position on an x-ray table will secure the roentgen details by fluoroscope or roentgenogram. It is not an evanescent, transitory pattern because it can be identified by succeeding films as long as the barium mucilage remains in the esophagus. No particular opaque mixture is required, although there are American proprietary products that are extremely smooth and easy to use. There is no necessity for advertised foreign opaque mixtures.

The mucosal pattern of esophageal varices is produced by the enlarged tortuous veins protruding into the lumen of this tube. The lumen may be widened if the varicosal condition is extensive. Varices can be pressed out by peristalsis and by increased intrathoracic pressure. Cancer and ulcer are easily differentiated from this characteristic varicose pattern by the usual extensiveness of the varices and the limited area of cancer or ulcer. The normal thin mucosal lines of the esophagus persist with cancer or ulcer except at the limited area of new growth, while with varicosal patterns the only normal lines are at the upper part of the esophagus. Varices are usually encountered with cirrhosis or fibrosis of the liver. Unrecognized cirrhosis has been inferred from this isolated and characteristic x-ray shadow. Esophageal varicosis is not an infrequent condition. One roentgenologist (Schatzki) found forty-five cases in two and one-half years.

Chronic hypertrophic gastritis provides enlarged, deep, stiff, thick rugae. Such rugae may be normal at the greater curvature of the pars cardiaca and media but are usually diagnostic of chronic gastritis at the pars pylorica and at the lesser curvature. Differential diagnosis is required for lymphoblastoma or cancer. Polypoid growths protrude into the gastric lumen. Increased mucous secretion produces a marbled appearance of the gastric contents. Nonopaque food residues and air bubbles offer little difficulty to the experienced eye. Extensive ulceration of the stomach is rare. The isolated ulcer or new growth is recognized by the identification of the actual lesion amidst an otherwise normal mucosal pattern.

Again, one can achieve this characteristic gastric diagnosis of enlarged, deep rugae by a thin mucilaginous opaque meal that is allowed by posture and compression to adapt itself to the gastric mucosa. Rolling the patient, forced breathing and moderate compression easily provide the pattern picture when roentgenograms are taken with the patient in favorable postures, both with and without pressure technic.

That I have focused attention on two particular uses of mucosal relief technic does not mean that its usefulness is thus confined. The point is that its usefulness beyond these two situations is reserved for the roentgen specialist who is equipped with experience, apparatus and training in the vagaries of the normal gastric and intestinal mucosa. The time required to complete the mucosal relief examination places it beyond or outside routine roentgen examinations. It is reserved for duodenal ulcers which are very small, for cases which offer technical difficulties of spasm, debatable niche formation, and for cases of stout or spastic type. Even among experts using this method there is the debatable field of active ulcer niche and healed scar, especially in the duodenum.

Kymography contrasts with the mucosal pattern technic in that it is entirely a record of function exhibited at a chosen margin of an organ. It is particularly useful for the study of the pulsating margin of the heart and aorta. There are many inherent errors and difficulties. The task of interpretation requires meticulous attention to shadow margin, and the personal equation of the roentgenologist looms large. Again, special apparatus is required. This fact, and the demands of special interpretation, seem to make kymography essentially the function of the qualified roentgenologist.

Kymography consists of placing a moving slit grid between the patient and the film during an exposure of an arbitrary time period. One must study the resulting surrealist exposure with caliper and rule to compare the recorded movement displayed by toothlike serrations at various, identified, moving margins of an organ. The cycle of cardiac movements is usually completed within a second plus; the patient can hold his breath and avoid the imposition of shadows of respiratory movements on cardiac movements.

The gastric motility is normally twenty-two seconds, and therefore respiratory and cardiac movements must be substracted from the essential gastric movements. This subtraction is very difficult. The value of kymography in gastric diagnosis would be for the study of the muscular movement of a portion of the wall where one suspected an early cancer. The method requires that the particular area be recorded by kymograph in profile. Gastric peristalsis must be functioning at the time; the opaque filling must be generous and perfect; the subtraction of respiratory movement may be possible, but cardiac movement is persistent during the briefest period of any practical gastric kymograph. Kymography, being a record of function or movement, must persist over a sufficient period of gastric peristalsis to permit analysis by mensuration of the movement of shadow margin. The method has no advantages over the fluoroscopic study of motion in the presence of a grossly visible ulcer or cancer. There are no advantages over the mucosal relief technic for the small lesion. The only advantage that kymography would add to diagnosis of early cancer is the study of the immovable area in the gastric outline. This area is comparable to the area in the ventricular or auricular wall that has

lost its usual muscular activity owing to extrinsic adhesions (cardiolysis) or intrinsic loss of tone (coronary infarction).

While there are no dangers to the roentgenologist in kymography of the stomach, there are the dangers to the patient of cutaneous reactions from the length and strength of the prolonged exposure required. Ordinary 1 mm. aluminum protection to the radiographic x-ray beam is not sufficient.

Enthusiasm for gastric kymography is not warranted. The theoretical possibilities are overshadowed by actual dangers of technic and physiologic embarrassments to interpretation.

These brief but critical objections to gastric kymography must not be confused with disparagement of the practical values of cardiac kymography. Cardiac kymography has many useful purposes and carries no dangers to patient or operator. It has been exposed by many excellent articles to the general and specialty groups. It was my enthusiasm for cardiac kymography and my hope for a method of estimating muscular embarrassment at small portions of the gastric wall in cases of early gastric cancer that led me astray. The mucosal relief study fails to identify movement and depends on actual morphologic defects. Gastroscopy enters the field of early diagnosis of gastric cancer with the best wishes of those who hope for positive identification of the lesion at a period when its complete ablation is a surgical practicality in a larger group of cases than seems possible now.

Professional Building.

ABSTRACT OF DISCUSSION

DR. LESTER LEVYN, Buffalo: Hirsch, Moore and Scott have shown the method to be of great value in the diagnosis of obscure cardiac lesions, but only a negligible amount of work has been done on the gastro-intestinal tract, particularly in this country. So far as the stomach is concerned the method is strictly in the experimental stage. The kymographic records are complicated and little is known about even the interpretation of the normal. Experience has been entirely too limited. I would hesitate to attempt to make a diagnosis of early carcinoma of the stomach by kymography that could not be made by our present methods. I am, however, optimistic about its future, and feel that within the next few years it may prove to be a procedure capable of detecting lesions earlier than can be done at this time. The study of the stomach and the esophagus by the mucosal relief method should be a routine procedure with every roentgenologist. Esophageal varices are diagnosed only rarely by a complete filling of the esophagus with barium sulfate. This is due to the fact that varices are hidden by the density of the opaque meal. The varices, however, certainly are more common than suspected and are more easily demonstrable when careful technic is carried out by the relief method. The veins are seen to project tortuously into the lumen of the esophagus. One should rarely miss esophageal varices when the relief method is employed and painstaking technic is required. Concerning chronic gastritis, the roentgen mucosal method may show the change that occurs in the hypertrophic variety in a fairly large percentage of cases, but it must not be forgotten that chronic gastritis may be present without any deviation from the normal in the mucosal pattern. When considering the question of atrophic gastritis, one is stepping on rather dangerous ground when one attempts to diagnose that condition, because the thin mucosal folds that may be indicative of atrophic gastritis are often seen in perfectly normal persons and also in certain persons suffering from blood dyscrasias, particularly pernicious anemia. The study of the rugae may disclose the presence of a peptic ulcer that may escape detection entirely when the usual contrast meal is given and, likewise, occasionally in relatively early carcinoma. Dr. Skinner's paper is valuable because he has so strongly stressed the advantages of study of the mucosal pattern. It often confirms or establishes a diagnosis when the large contrast meal fails to do so. It is, however, advisable to conduct gastrointestinal examinations by both methods.

DR. WENDELL G. SCOTT, St. Louis: Dr. Skinner has ably surveyed the field of kymography in the study of gastric lesions. Dr. Sherwood Moore and I have used the method in a few cases. The kymographic method in gastro-enterology is limited by the slow movements of these structures and by the long exposure time. The method at this stage is not a practical clinical procedure. It can be used for experimental work, particularly in a painstaking investigation of the movements of the rugae, gastric silhouette and duodenum.

YELLOW BONE MARROW EXTRACTS IN GRANULOCYTOPENIA

PRELIMINARY REPORT

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AND
H. O. WILES, PH.D.
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At the Milwaukee session of the American Medical Association, in 1933, Dr. C. H. Watkins of the Mayo Clinic announced that he had obtained favorable results on treating patients suffering from granulocytopenia with yellow bone marrow. He reported that a monocytosis first occurred, which was followed by a gradual increase in polymorphonuclear neutrophils. Usually a reaction occurred within twenty-four to forty-eight hours after ingestion of the bone marrow. An account of this work has not yet been published by Dr. Watkins.[1]

Shortly after this announcement Dr. M. J. Flipse of Miami, Fla., also obtained very encouraging results with the marrow but found that the large dose which is necessary was undesirable, and it was through his suggestion and that of Dr. Fenger of Armour & Co. that we sought to prepare an extract which would be free of the large amount of fat that is present in the refined marrow. Such a concentrate was prepared by extracting the unsaponifiable portion of the marrow and dissolving it in a bland oil for oral administration. The equivalent concentration of 2 Gm. of marrow per drop has been found quite satisfactory for clinical use.[2]

There being as yet no satisfactory method for producing agranulocytosis in experimental animals, it has been necessary to test the activity of our preparations on the occasional clinical cases that have been available. We are greatly indebted to the physicians who have cooperated with us in this phase of our work.

Up to the present time the extract has been administered to twenty patients with granulocytopenia, and in all but seven there has been a rise in the number of granulocytes, usually with a return to normal figures. In fact, if active infection persists during the period of treatment the granulocytes may rise to figures far above normal. Of the seven patients who did not give a satisfactory response, two were later found to have

From the Otho S. A. Sprague Memorial Institute and the Department of Pathology, University of Chicago.

1. Dr. Watkins has published an account of the use of bone marrow in anemia (J. A. M. A. **95**: 587 [Aug. 23] 1930) in which he reported a remarkable response in one case of agranulocytic angina.

2. Recently there has appeared a paper by Joseph Zichis (Granulocytopoietic Fractions of Yellow Bone Marrow, J. Lab. & Clin. Med. **22**: 231-237 [Dec.] 1936), the data of which indicate that he partially saponified the marrow, removing only part of the fat. He does not acknowledge our prior work (paper read before the Medicinal Section of the American Chemical Society, Cleveland, Sept. 11, 1934), which was reported in preliminary form in 1934. His experimental work and method of testing, which was carried out on rabbits, will be criticized in more detail when this work is published in full.

aplastic anemia; in four a differential diagnosis was not made, and the last had diabetes and appendicitis in addition to the granulocytopenia. The rise in granulocytes usually begins within twenty-four to thirty-six hours, as contrasted with the effect of pentnucleotide, which is not usually manifested in less than from four to five

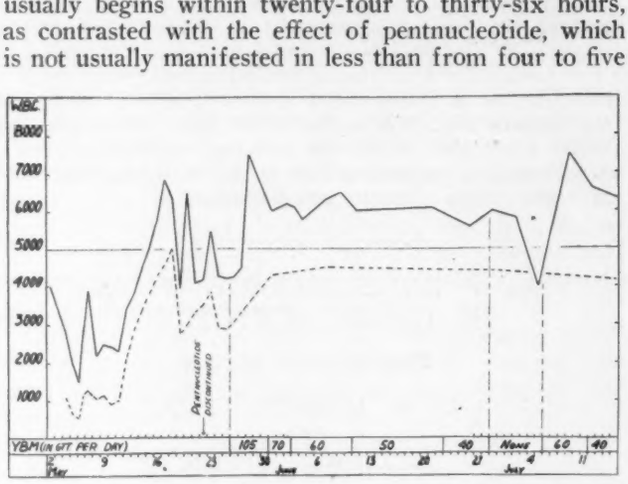

Chart 1 (case 1).—Response of leukocytes (solid line) and neutrophils (dotted line) to yellow bone marrow.

days. We are informed by Dr. Flipse, who has used our concentrate in several cases, that he has obtained similar results.

To illustrate the characteristic effects of the bone marrow extract, brief abstracts of two typical cases are presented:

CASE 1.—Miss E. D., a patient of Dr. Maurice Simkin, was diagnosed as having "agranulocytic angina." Chart 1 indicates slight but transitory response to pentnucleotide together with liver extract and "extralin." The patient objected to her reactions to pentnucleotide, saying that she would "rather die than have another injection," whereupon all medication was discontinued in favor of yellow bone marrow. Two enteric coated capsules (0.5 Gm. each) of the nonsaponifiable residue were given each of two days. There was no response. It was later learned that the capsules were too heavily coated and would not open in the gastro-intestinal tract. When the oil solution was used orally a prompt response was obtained—within thirty-six hours—and a maintenance dose could be established. When the extract was discontinued the count fell immediately but increased rapidly again on resumption of

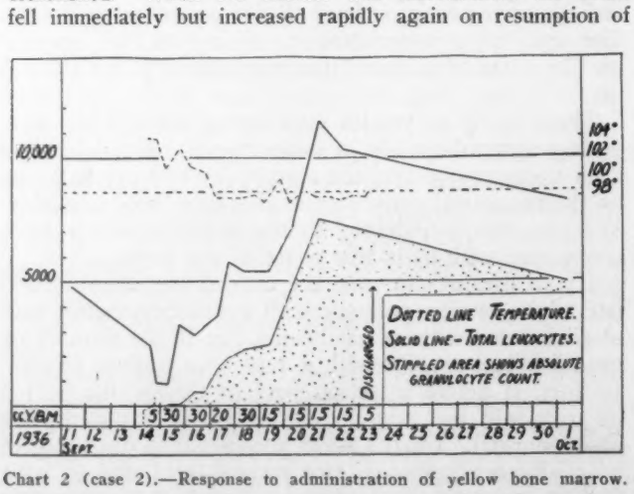

Chart 2 (case 2).—Response to administration of yellow bone marrow.

medication. The granulocyte/lymphocyte ratio also became normal on extract therapy. Clinical improvement was coincidental with the improvement in the blood picture, and she was discharged. The patient had a recurrence in March 1937 but improved rapidly when given the extract. A response almost identical with the responses recorded in chart 1 was obtained, and the angina cleared up within seventy-two hours, the leukocyte count rising from 3,500 to 7,500 on medication with the extract.

CASE 2.—Mrs. M. J. had been seen occasionally in the outpatient service of the Chicago Lying-in Hospital with a complaint of menorrhagia and dysmenorrhea. She had been taking a proprietary medicine containing aminopyrine for the latter. When examined Sept. 11, 1936, she showed no remarkable symptoms except those mentioned. The leukocyte count was 4,800 (chart 2).

She was admitted for treatment September 14, with acute tonsillitis and pharyngitis, a temperature of 104 F., and a leukocyte count of 2,400, which fell later to 925. A diagnosis of probable agranulocytic angina was made and yellow bone marrow extract therapy was begun immediately; no other hematopoietic stimulant was given.

The following morning the count was between 700 and 1,000 white blood cells (3 per cent neutrophils) but had risen by evening (twenty-four hours from the beginning of treatment) to 3,300 white blood cells, 83 per cent lymphocytes, 12 per cent monocytes, 1 per cent metamyelocytes, 2 per cent band forms and 2 per cent segmented neutrophils. The temperature had fallen to normal by September 17; clinical improvement followed immediately on the improving blood picture. The peak of the bone marrow response was reached September 21, with 11,500 white blood cells and 65 per cent neutrophils, of which 52 per cent were segmented, 12 per cent band form and 1 per cent myelocytes and metamyelocytes. The patient was discharged in good condition September 23. Subsequent blood counts were within normal limits.

A more detailed report of the chemical work and clinical observations will be presented in a subsequent paper.

THE DIAGNOSIS AND TREATMENT OF UNDULANT FEVER

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AND
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The purpose of this paper is to discuss briefly the diagnosis and treatment of undulant fever. Time does not permit a full review of all the therapeutic measures which have been offered; therefore our remarks will be limited mainly to a further discussion of the use of intravenous injection of killed typhoid and paratyphoid organisms in the treatment of this disease.

The diagnosis of undulant fever is dependent on the laboratory for final confirmation. In this connection certain diagnostic problems confront the physician. The patient may present some of or all the classic symptoms, namely, irregular fever, profuse night sweats, weakness, nervousness, epigastric pain, nausea, vomiting, arthralgia and, in addition, some complication, such as involvement of the central or the peripheral nervous system or suppurative arthritis, and yet the blood may show no agglutination for organisms of the brucella group. This negative reaction may be due to the insufficient lapse of time for the development of specific agglutinins. The length of time varies widely, usually from two to several weeks. However, the agglutination may never at any time become positive.

A positive agglutination reaction must always be correlated with the symptoms and physical signs shown by the patient. There are numerous reports in the literature of the presence of Brucella agglutinins in the blood of persons who have no other evidence of disease. One of us (Hunt)[1] in a study of 1,000 unse-

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1. Hunt, H. F., and Noll., M. E.: A Study of Native Agglutinins for Brucella in Human Blood Sera, Pennsylvania M. J. **40**: 433-435 (March) 1937.

lected samples of blood found 8.9 per cent of the serums to agglutinate specific Brucella antigens in a dilution of 1:80 or above. An analysis of clinical and other laboratory observations on this group of patients will be published at a later date. One can only conjecture as to the origin of such agglutinins. Many theories have been advanced to explain their presence in the blood of apparently normal persons, but to date none of the theories have been definitely proved or accepted. Veterinarians, packing house workers and breeders of live stock often are found to have positive agglutinins in their blood. Their presence is thought to indicate a past infection or recent exposure to infected materials.

The determination of opsonocytophagic power of the blood for Brucella is another laboratory procedure that may be employed in the diagnosis of undulant fever. A fresh bacterial suspension prepared each day from a pure culture of organisms of the Brucella group is essential for this test. Any one of the three specimens of Brucella is suitable, but the cultures should be checked frequently for "fastness" to phagocytosis. It occasionally happens that strains of Brucella tend to become fast to ingestion by cells.

Huddleson, Johnson and Hamann [2] have reported a method for determining the opsonocytophagic power of the blood which is a modification of the Leishman [3]-Vetch [4] technic. The method of recording phagocytic activity as outlined by the first mentioned authors consists of counting a total of twenty-five cells in different sections of the spread and recording each cell as follows: negative when no phagocytosis occurs, slight when from one to twenty bacteria are seen in the cell, moderate when from twenty-one to forty bacteria are seen in the cell and marked when the number of bacteria in the cell is above forty.

The interpretation of the results obtained by this test in the hands of the inexperienced may be as misleading as the results of the agglutination test. A more detailed report on this procedure will be found in Huddleson, Johnson and Hamann's [2] article and in Huddleson's [5] monograph on "Brucella Infections in Man and Animals."

Blood culture is helpful in many instances but as a diagnostic measure is slow. Special equipment is required and will not be found in many laboratories. The absence of leukocytosis is helpful. In fact, there may be leukopenia. We have usually found a normal differential count.

We believe that the intradermal test either with a Brucella abortus vaccine in a 1:10 dilution or with soluble nucleoprotein fraction of similar origin is helpful in diagnosis. The reaction must be regarded as negative unless it remains positive for a week or ten days (fig. 4). Frequently the reaction remains positive for eight or ten weeks, and the fading mark may be visible for a year. Too strong a solution is to be avoided lest central necrosis develop at the site of injection. The intradermal test depends on tissue sensitivity induced by the presence in the body of organisms of the Brucella group. A positive reaction may result from frank Brucella infection or from repeated small infections inadequate to produce fever. So, too, this test is invalidated unless it is supported by active symptoms.

Enthusiasm for making a diagnosis of brucellosis may cause the physician to overlook such common infections as tuberculosis, typhoid fever, subacute bacterial endocarditis, hidden malignant growths, rheumatic fever, otitic infections in children and less common conditions such as meningococcic septicemia. Perhaps the most useful procedure is to entertain the diagnosis of brucellosis in all cases of unexplained fever or prolonged disability, especially of the neurasthenic type.

The behavior of the temperature shows the widest variations from sudden onset with high elevation to an insidious beginning, barely noticeable to the patient. Two of our twenty-two patients showed sudden onset with regularly recurring chills. In one instance the chills occurred every forty-eight hours and in the other every seventy-two hours. Perhaps the most characteristic thing about the fever is the constant irregularity, so that it need not be confused with that of typhoid, empyema, tuberculosis or other common infections.

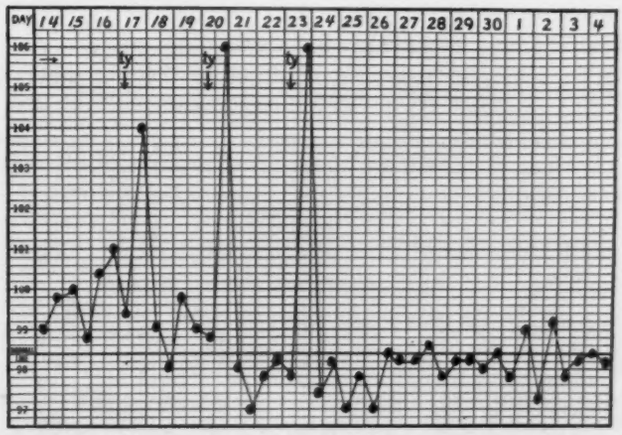

Fig. 1 (case 1).—The high and the low temperature in twenty-four hours before, during and after treatment. Although fever had been present for seven months, recovery was prompt and complete.

TREATMENT

One finds in reviewing the literature that most successful treatments are accompanied by a sharp thermal reaction. This is true regardless of whether the treatment given is administration of a vaccine, toxic filtrate, specific serum, chemical or foreign protein or fever induced by mechanical appliance.

Debono [6] noted that after intravenous injection of filtrate prepared from brucellin and melitine the temperature reached a maximum in seventeen or eighteen hours and then fell the following day. After two or three such treatments he was able to reduce the temperature to normal. In one of our cases a favorable drop in temperature occurred after the sharp thermal reaction induced by mercurochrome injected intravenously and sterilized skimmed milk injected intramuscularly. Prickman and Popp [7] used the Simpson-Kettering Hypertherm to induce fever in three cases of brucellosis. The results, while somewhat delayed, were generally satisfactory. Carpenter

2. Huddleson, I. F.; Johnson, H. W., and Hamann, E. E.: Study of the Opsonocytophagic Power of the Blood and Allergic Skin Reaction in Brucella Infection and Immunity in Man, Am. J. Pub. Health **23**: 917-929 (Sept.) 1933.
3. Leishman, W. B.: Studies on Phagocytosis, Tr. Path. Soc. London **56**: 344, 1905.
4. Vetch, R. M.: A Simple and Rapid Method of Estimation of the Phagocytic Power of Different Bloods, J. Path. & Bact., **12**: 353, 1908.
5. Huddleson, I. F.: Brucella Infections in Man and Animals, New York, Commonwealth Fund, 1936.
6. Debono, J. E.: Treatment of Undulant Fever, Lancet **1**: 374-375 (Feb. 16) 1935.
7. Prickman, L. E., and Popp, W. C.: Treatment of Brucellosis by Hyperpyrexia Induced by the Simpson-Kettering Hypertherm, Proc. Staff Meet., Mayo Clin. **11**: 506-510 (Aug. 5) 1936.

and Boak,[8] in a review of the treatment of human brucellosis, aptly remarked that the attribution of favorable results to a specific effect of the vaccine is not justifiable. In their opinion the good results depend on the intensity of the generalized systemic reaction evoked by the injection, the type of vaccine playing little part. These authors, further, added a word of caution regarding the possible toxic action of the vaccines. It must be noted, however, that numerous cures have been reported when no thermal reaction was induced by the medicament. One must not forget that spontaneous recovery often takes place. In this connection we quote from one of our colleagues with whom we had discussed fever therapy for a case of active brucellosis. She wrote: "Our patient had such a complete remission (the temperature dropped from 104 F. to normal, with complete subsidence of all symptoms) that we were not justified in using typhoid vaccine. If I had used the vaccine a week sooner we would have thought it a fine remedy." Had this correspondence occurred earlier, the patient would likely have been added to the list of those successfully treated by a certain method.

REPORT OF CASES

The following cases, in addition to the ten others already reported, represent our experience with the use of mixed typhoid vaccine[9] injected intravenously.[10] We include one control case, in which this agent was not used.

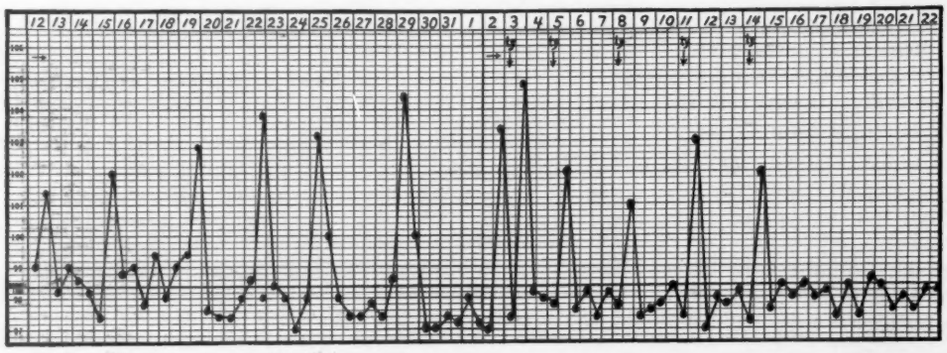

Fig. 2 (case 2).—The high and the low temperature in twenty-four hours, before, during and after treatment. Recovery was prompt and complete. This chart illustrates regularly recurring paroxysms of chills and fever.

CASE 1.—T. V., a man, aged 30, an undertaker, admitted Sept. 14 and discharged Sept. 26, 1936, became ill seven months before admission with sudden fatigue, followed by low grade fever and gastro-intestinal distress, loss of appetite, furred tongue and chronic constipation, tenderness over the right upper quadrant, bloating and the loss of 31 pounds (14 Kg.). Physical examination was not helpful beyond revealing evidence of the loss of weight. The temperature ranged from 100 to 101 F. Agglutination was negative, the intradermal reaction strongly positive. Treatment consisted of three injections of typhoid vaccine, 30 million organisms. The temperature (fig. 1) remained normal after the third injection, and recovery was prompt and complete. The illness lasted thirty-two weeks; it terminated two weeks after treatment. At a follow-up examination May 9, 1937, agglutination was negative and the intradermal reaction moderately positive.

CASE 2.—H. F., a man, aged 19, a garage mechanic, admitted July 12 and discharged Aug. 21, 1936, became ill three weeks before admission with chills which occurred quite regularly every two to four days, sweats, pain in the ribs and headaches. Physical examination gave entirely negative results. He had four chills after admission, at seventy-two hour intervals. On July 13, the twenty-second day after the onset of illness, agglutination for Brucella abortus was negative, but nine days later it was found to be positive in a titer of 1:200. The leukocytes numbered 5,500 and the neutrophils 71 per cent. Treatment consisted of seven injections of typhoid vaccine, from 50 to 80 million organisms. The temperature dropped to normal after the first injection, and the patient had no more chills (fig. 2). He recovered completely and returned to work on the day after he was discharged from the hospital. The illness lasted five weeks. At a follow-up examination May 9, 1937, the weight was 160 pounds (72 Kg.), a gain of 30 pounds (13 Kg.). Physically the patient was entirely normal. Agglutination was negative in all dilutions. The intradermal reaction was negative.

CASE 3.—F. L. P., a man, aged 37, a minister, admitted Jan. 8 and discharged Jan. 25, 1937, had been ill twenty-six days. The onset was gradual with generalized pains in the body associated with chilly sensations and a temperature from 102 to 104 F. The patient was nauseated and vomited the first few days. He had a constant dull headache and several attacks of vertigo and fainted once. He had no pains in the joints but felt feverish and extremely weak. Physical examination was not helpful. A blood count showed hemoglobin 84 per cent, red blood cells 5,320,000, leukocytes 11,150, neutrophils 61 per cent, eosinophils none. Agglutination was negative for Brucella abortus. The intradermal reaction was strongly positive; the temperature varied from 100 to 101.4 F. for one week. The treatment consisted of two injections of 30 million typhoid organisms. The temperature was normal after the first injection. The patient returned to work February 17. The illness lasted eight weeks, four weeks after treatment. At a follow-up examination May 13, agglutination and the intradermal reaction were negative.

CASE 4.—G. W. L., a man, aged 45, a farmer, admitted June 14 and discharged June 19, 1936, readmitted Sept. 18, 1936, and discharged October 14, became ill six months before admission, with grip. This was followed shortly by chills, fever, sweats, headaches, backache, malaise and generalized stiffness of joints and loss of 11 pounds (5 Kg.). Physical examination was not helpful. Agglutination for Brucella abortus was positive in a titer of 1:500. The temperature on admission was 99.4 F. It promptly returned to normal, and we thought the patient was experiencing a natural remission, so he was allowed to go home untreated. His fever returned, and the other symptoms failed to clear up. After a second admission he was given seven injections of from 30 to 127 million typhoid organisms. Since he left the hospital his temperature has remained normal and he has been free from symptoms except for nervousness, which is quite unnatural for him. The illness lasted thirty-two weeks. At a follow-up examination May 12, 1937, agglutination for Brucella abortus was positive in a titer of 1:500, the intradermal reaction was ++ and the weight was 154 pounds (70 Kg.), a gain of 17 pounds (8 Kg.). The patient said "I can't do a day's work, my legs give out." There was slight dyspnea on exertion. The results were only fair.

CASE 5.—R. W., a man, aged 18, a student, admitted Sept. 13 and discharged Sept. 18, 1936, became ill August 1 with lethargy, loss of weight, lack of ambition, loss of appetite, frontal headache, pain in the legs, chills and a rise of temperature in the afternoon for one month. He had such profuse night sweats one week that he frequently had to change his

8. Carpenter, Charles M., and Boak, Ruth A.: Treatment of Human Brucellosis, Medicine **15**: 103-127 (Feb.) 1936.
9. Eli Lilly & Co. no. 3V765.
10. Ervin, C. E.; Hunt, H. F., and Niles, John S., Jr.: Foreign Protein Therapy: II. Treatment of Undulant Fever by the Intravenous Injection of Killed Typhoid-Paratyphoid A and Paratyphoid B Bacilli, Am. J. M. Sc. **192**: 234-241 (Aug.) 1936.

night clothes. Physical examination was not helpful. The leukocytes numbered 3,600. The temperature varied from 99 to 103 F. Agglutination for Brucella abortus was positive in a titer of 1:500. The treatment consisted of an injection of 40 million typhoid organisms September 17 and two similar injections after the patient returned home. The temperature was normal after September 20. The patient was ill twenty-seven days before treatment was begun and had an immediate recovery. May 12, 1937, he was in perfect health and physical

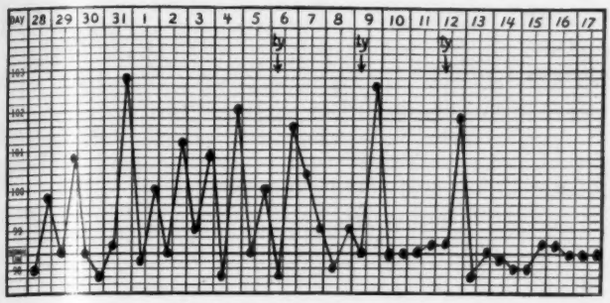

Fig. 3 (case 9).—The high and the low temperature in twenty-four hours. The temperature returned to normal after the second injection. Recovery was prompt and complete.

examination gave entirely negative results. He had gained 30 pounds (13 Kg.). Agglutination was positive in a titer of 1:500. The intradermal reaction was moderately positive.

CASE 6.—H. B., a man, aged 43, an undertaker, admitted April 2[illegible] and discharged May 21, 1937, had been ill four months with weakness and nervousness which rendered him almost unable to carry out his work, chills and sweats, continuous pains in the joints but no swelling, pain in the region of the right sciatic nerve and weakness in the right sacro-iliac joint. He said "I am sore all over: my flesh is like a raw piece of meat." Examination showed that he was apprehensive and fairly well nourished, with chronic tonsillitis, periapical dental infection and tenderness over the right sacro-iliac joint. The temperature ranged from normal to 101.2 F. Agglutination for Brucella abortus was positive in a titer of 1:160. Treatment consisted of four injections of typhoid vaccine, from 60 to 160 million typhoid organisms, and tonsillectomy. With the exception of nervousness, unnatural to him, the symptoms completely disappeared in sixty days. May 12, agglutination was negative and the intradermal reaction strongly positive. The patient was still nervous.

CASE 7.—S. M., a nun, aged 27, admitted July 3 and discharged Aug. 31, 1936, had been ill six months. The illness began with nervousness, occasional night sweats and frequent excessive perspiration during the day, constant pain in the region of the right sciatic nerve and loss of 12 pounds (5 Kg.). At physical examination she was practically afebrile and had slight nasal and pharyngeal congestion and tenderness over the right sciatic nerve. Agglutination for Brucella abortus was positive in all dilutions. Treatment consisted of one month of rest in bed and six intravenous injections of typhoid vaccine, from 30 to 90 million organisms. The results were not immediately helpful, and the benefits from treatment are doubtful, although all symptoms disappeared during the following ninety days.

CASE 8.—S. L., a woman, aged 34, a school teacher (patient of Dr. Ralph W. Thumma, Schaefferstown, Pa.), in September 1936 began to have sleeplessness, irritability, nervousness, especially in the morning, and fatigue. She was tired on arising in the morning and found it hard to do any work. Gradually her appetite disappeared, and she lost 27 pounds (12 Kg.) and had a low grade fever. She was seen first Nov. 16, 1936. Physical examination was not helpful except to provide evidence of the loss in weight. Laboratory examination showed red blood cells 3,800,000 and leukocytes 7,750. The temperature ranged from 99 to 100 F. Agglutination for Brucella abortus was positive in a titer of 1:80. The patient was hospitalized Jan. 4, 1937, and given 10 million mixed typhoid organisms intravenously. The injection was repeated January 9, and the temperature dropped to normal; it remained so for one month and then varied from 99 to 103 F., the fever being accompanied by chills. February 9 the patient was given 30 million typhoid organisms intravenously and five days later a dose of 50 million. The temperature promptly returned to normal. May 14, 1937, the patient had not gained weight but was relieved and was improving so far as the symptoms of undulant fever were concerned.

CASE 9.—W. R., a man, aged 23, a grocery clerk, admitted Aug. 28 and discharged Sept. 1, 1936, became ill three weeks before admission with a tired feeling in the legs and a rise of temperature in the afternoon to from 101 to 102 F. Physical examination was not helpful. Agglutination for Brucella abortus was positive in a titer of 1:500. Treatment consisted of three injections of from 30 to 40 million typhoid organisms. The temperature remained normal after the first treatment (fig. 3). Convalescence was complete, and the patient has since been symptom free. He returned to work Oct. 1, 1936. At a follow-up examination, agglutination was positive in a titer of 1:500 and the intradermal reaction positive.

CASE 10.—I. L. F., a man, aged 45, a veterinarian, admitted May 11 and discharged May 26, 1936, had typical undulant fever in 1929 with strongly positive agglutination. In that attack he had pain in the shoulders, vague abdominal distress, headache and "giant urticaria." He contracted the disease while caring for herds infected with Bang's disease. He had a fever for nearly a year and never recovered his health. On admission, seven years after onset, he still complained of pain in his shoulders and intercostal areas; in fact, he had been unable to carry on his business. He complained of annoying paresthesia, especially in the right elbow and the right thigh. It was not deemed advisable to give him typhoid vaccine on account of the duration of his illness.

Fig. 4 (case 4).—A positive reaction ten days after an intradermal injection of 0.1 cc. of a 1:10 dilution of undulant fever vaccine.

COMMENT

It will be noted that the course of acute and subacute Brucella infection was apparently shortened by this method of fever therapy.

It is of interest that in our small series of twenty-two patients one finds three invalids, all with chronic infection of from one to seven years' standing (cases 11 and 12 of a former report and case 10 of this report). The second patient, a woman 51 years of age, was given treatment in August 1935 and did well in spite of her age and her illness of nearly one year until February 1937, when definite psychasthenia developed, which has incapacitated her as a housewife. Patient 10 of this series is an example of an untreated person now a sufferer from a neurasthenic condition, a common complication, as pointed out by several authors. Such complications should cause no surprise when one recalls the frequency of definite involvements of the central

nervous system in undulant fever. They include meningitis, encephalitis and various forms of neuritis.

The mechanism of recovery is still a speculation, as pointed out in previous communications.[11] We reported that from the hemocytologic standpoint the most significant changes which occurred after the intravenous injections of killed typhoid and paratyphoid bacilli were found in the total leukocyte, the neutrophil, the metamyelocyte and the lymphocyte count. These observations were made by obtaining a control count immediately before the injection of killed organisms. After the injection of the killed typhoid and paratyphoid bacilli complete blood counts were made at hourly intervals for a period of four hours; twenty-four hours after the injection was made another complete blood count was taken. With a few exceptions the blood counts were made by the same person, and the differential counts in all instances were checked by one of us.

In the series of cases reported in this article a similar study was made of each patient's blood, and in every instance after the injection of the killed organism relative leukopenia occurred in the first hour followed by a return to the preinjection level after twenty-four hours. The response of the neutrophils closely paralleled the response of the total leukocytes. The metamyelocytes showed no initial increase but a steady increase during the first four hours.

The lymphocytes showed an increase in the first hour and a decrease in the following three hours. The post-injection twenty-four hour count revealed that the lymphocytes were near the preinjection level. All the hemocytologic changes were transient, as evidenced by the fact that at the end of twenty-four hours the observations were practically identical with the preinjection observations.

While the observations reported in this study do not explain why the patients recovered, we do feel that as they were infected with a specific organism the results obtained strengthen the theory that the injection of killed typhoid and paratyphoid bacilli stimulates a general nonspecific immunogenic reaction. This reaction is reflected in the altered blood picture, which indicates a response of the reticulo-endothelial system to the foreign proteins injected.

Such response may in turn be the fundamental reaction which is responsible for the production of resistance or immunity. While we do not know exactly where antibodies are formed, our results suggest that the injection of killed typhoid and paratyphoid organisms is responsible for the production in the body of nonspecific antibodies of sufficient quality to enable the patient to overcome the disease. Of course one cannot discuss immunity without considering the rôle of the phagocytes in ridding the body of bacteria.

We do not maintain that injection of typhoid vaccine is the ideal treatment, but we do feel that it is the most practical method available to the rank and file of physicians who find here and there a case of brucellosis. It saves the necessity of trying to locate the specific vaccine or serum and more cumbersome methods of inducing fever. We have no hesitancy in advancing this form of treatment in view of the fact that, whatever the method used, the benefit seems to depend on thermal reaction. Its contraindications, namely, advanced arteriosclerosis, arteriosclerotic or rheumatic heart disease, and marked debility, are common to other forms of therapy.

11. Hunt, H. F.; Ervin, C. E., and Niles, John S., Jr.: Foreign Protein Therapy. I. Hemocytologic Changes following the Intravenous Injection of Killed Typhoid-Paratyphoid A and Paratyphoid B Bacilli, Am. J. M. Sc. **189**: 95-102 (Jan.) 1935; footnote 10.

CONCLUSIONS

1. The results in the treatment of acute and subacute undulant fever by the intravenous injection of killed typhoid and paratyphoid organisms in carefully measured and appropriate doses compares favorably with those of any other form of treatment.

2. Contraindications to its use are arteriosclerosis, arteriosclerotic and rheumatic heart disease, hypertension and marked debility. These conditions also contraindicate most other forms of treatment.

3. We agree with Carpenter and others that the benefit comes chiefly from fever, but the stimulation of antibodies may also be important.

4. The advantage is the low cost and the immediate availability to any physician anywhere.

ABSTRACT OF DISCUSSION

DR. WALTER M. SIMPSON, Dayton, Ohio: Soon after our studies in undulant fever were begun in 1928, we experimented with the therapeutic use of a Brucella melitensis-abortus vaccine. We pointed out that the vaccine was effective only in patients who responded with at least three or four sharp febrile reactions, which usually occurred after the dosage of the vaccine had reached from 0.5 to 1 cc. In 1932 a woman missionary who had acquired undulant fever while resident in China was sent to us for treatment. A goat was the source of the fever. Vaccine therapy did not provoke the usual febrile response. She was then given two artificial fever treatments, each of five hours' duration, at 105 F., rectal temperature. All evidence of undulant fever promptly disappeared. She returned to her work in China and has remained well since. It would appear that in all of these methods, including the foreign protein method just described, the production of fever artificially is the common denominator. Through correspondence with the collaborators in the experimental work in artificial fever therapy inaugurated by the Kettering Institute, I have learned of more than a score of cases of undulant fever which have been treated with artificially induced fever with uniformly favorable results. One might ask how it happens in a disease characterized by sharp febrile reactions that artificial fever therapy would be effective. It would appear that the prolongation of the fever at a relatively high level stimulates immune reactions. It has been our practice to treat such patients at 105 F., rectal temperature, for four or five hours at each session, at intervals of two to three days. In most cases, two or three treatment sessions will suffice. If the production of sustained artificial fever is the important factor in the treatment, it seems logical to conclude that those methods which permit the production of fever under relatively safe and controlled conditions would be the methods of choice. The advent of simpler and safer methods for the controlled production of fever by mechanical means, when administered by skilled, trained workers, provides such a method. The injection of protein or chemical substances provokes less constant febrile responses and occasionally produces untoward reactions. Our present practice is to give a trial course of Brucella melitensis (abortus) vaccine therapy (N. N. R.). If it is ineffective, we then utilize artificial fever therapy (Kettering hypertherm method). After we had reported 148 cases of undulant fever in and about Dayton, Ohio, an ordinance requiring the pasteurization of all milk and dairy products was passed. During the five years since the passage of that ordinance, not one case of undulant fever has originated in Dayton, Ohio. In any consideration of the treatment of undulant fever, the best treatment is still to prevent the disease by eliminating the sources of infection.

DR. CARL E. ERVIN, Danville, Pa.: Dr. Simpson's remarks are very helpful in this discussion. I agree with him that fever therapy induced by various mechanical means will probably help out in the treatment of a great many of these cases of undulant fever. Of course, the thing I like about typhoid

vaccine is that it is available to every doctor and he can use it himself. I feel sometimes that it is rather a stimulus to a doctor to feel that after all he can do something himself. The remark about prevention is certainly in order. In the city of Wilkes-Barre, Pa., for instance, I understand that there has not been a case of undulant fever, as the result of rigid food inspection. It should be carried out in every rural district and city of the country.

DIAGNOSTIC METHODS IN UNDULANT FEVER (BRUCELLOSIS)

WITH RESULTS OF A SURVEY OF 8,124 PERSONS

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AND
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The purposes of this paper are (*a*) to describe briefly the performance and interpretation of the laboratory methods which at present are believed to be most useful in the diagnosis of undulant fever (brucellosis) and (*b*) to report some of the results of a survey of the incidence of brucellosis in a large county hospital.

LABORATORY METHODS

The laboratory methods which are regarded as most useful are (1) the brucellergin intradermal test, (2) the opsonic (opsonocytophagic) test (3) the rapid agglutination test and (4) culture (isolation) of Brucella.[1]

Fig. 1.—Positive brucellergin test. Note extensive areas of edema.

1. The brucellergin test is performed by injecting 0.1 cc. of a suspensoid of nucleoprotein (1:2,000) isolated from Brucella cells intradermally on the forearm and is read after forty-eight hours (fig. 1).

2. The brucella opsonic test is performed by incubating a mixture of a live forty-eight hour culture of Brucella abortus and the patient's citrated blood in a water bath at 37 C. for thirty minutes. The mixture consists of 0.1 cc. of a saline suspension of organisms having a turbidity of 6 mm., as measured by the Gates apparatus, and 0.1 cc. of the patient's citrated blood having a dilution of 0.8 per cent citrate (5 cc. of blood added to 0.2 cc. of 20 per cent sodium citrate in saline solution). A smear of the mixture is then made on a glass slide, rapidly dried with an electric fan and treated with 0.5 cc. of Hasting's stain for thirty seconds, after which 1 cc. of distilled water having a p_H of 6.4 is added for ten minutes. Twenty-five polymorphonuclear leukocytes are examined and their opsonic power classified according to the number of brucella organisms counted within each cell, as follows: negative, no phagocytized bacteria; slight, from 1 to 20; moderate, from 21 to 40, and marked, over 40 (fig. 2).

3. The rapid agglutination test is done on a glass plate that is ruled off into inch squares and rests on a dark field illumination box. In each of five squares the following respective amounts of patient's serum are placed: 0.08 cc., 0.04 cc., 0.02 cc., 0.01 cc. and 0.004 cc. A standardized dropper being used, 1 drop of rapid antigen is added to each amount of serum, to form respective serum concentrations of 1:25, 1:50, 1:100, 1:200 and 1:500. The contents of each of the five squares are then thoroughly mixed with a clean toothpick, the operator proceeding in reverse order from the 1:500 to the 1:25 serum concentration. The glass plate is removed from the box, tilted backward and forward slowly for about two minutes and then replaced on the box. The light is now turned on and the results read (fig. 3).

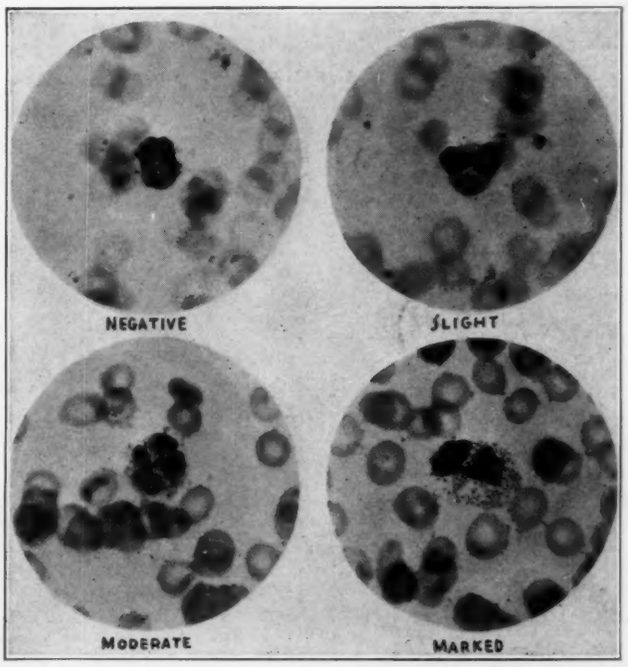

Fig. 2.—Brucella opsonic test, showing polymorphonuclear leukocyte with negative, slight, moderate and marked phagocytosis of Brucella organisms.

4. Culture (isolation) of Brucella is done as follows: (*a*) In taking a blood culture, 10 cc. of blood is added to 10 cc. of sterile 4 per cent sodium citrate in saline solution and incubated at 37 C. for twenty days in a jar in which 10 per cent of the air has been displaced by carbon dioxide (fig. 4). The uncoagulated whole blood serves as a highly satisfactory medium for the isolation of Brucella, while the final concentration of 2 per cent sodium citrate serves to retard the action of opsonins if they are present in the blood. At four day intervals the jar is opened and 0.5 cc. of blood-citrate

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From the Departments of Pathology of Eloise Hospital, Eloise and Wayne University College of Medicine, Detroit, and the Department of Bacteriology, Michigan State College, East Lansing.
1. Huddleson, I. F.: Brucella Infections in Animals and Man, New York, Commonwealth Fund, 1934. Keller, A. E.; Pharris, Crit, and Gaub, W. H.: Diagnosis of Undulant Fever, J. A. M. A. **107**: 1369 (Oct. 24) 1936.

mixture is removed and inoculated on a liver agar slant.[2] The freshly inoculated agar slant is also incubated in the 10 per cent carbon dioxide atmosphere. At each four day interval, all culture tubes are examined for growth (fig. 5).

(*b*) Specimens of urine, stool, bile, spinal fluid or other infective materials are prepared for culture according to standard methods. Such material is inoculated on plates of liver agar containing gentian violet in a concentration of 1:200,000. One half of the plates are incubated aerobically for ten days; the other half are placed in a container having a 10 per cent carbon dioxide atmosphere and incubated at 37 C. for three days.

INTERPRETATION OF RESULTS

1. The brucellergin test is negative if erythema alone is present. A negative test will usually rule out brucellosis. The brucellergin test is positive if in addition to an area of redness there is also edema or induration which measures from 0.5 to 7.5 cm. or more in diameter. A positive test is specific for sensitization to Brucella and is due to past or present infection. It does not, however, indicate the patient's immune status, which may then be obtained by the opsonic test.

2. The brucella opsonic (opsonocytophagic) test in a subject reacting negatively to the intradermal test will almost always show little or no phagocytosis. A subject reacting positively to the intradermal test is classified as infected when less than 40 per cent of his polymorphonuclear leukocytes show marked phagocytosis and as infected but with questionable immunity if from 40 to 60 per cent of his polymorphonuclears show marked phagocytosis. A subject reacting to the intradermal test is classified as immune when 60 per cent or more of his polymorphonuclear leukocytes show marked phagocytosis of Brucella organisms.

TABLE 1.—*Results of Brucellergin Intradermal Tests on Various Groups, Eloise Hospital, 1935-1936*

Group	Number of Tests	Number Positive	Percentage Positive
Hospitalized patients	815	51	6.2
Indigent persons	3,698	279	7.0
Indigent food handlers	439	39	8.8
Employees	778	106	13.6
Mental patients	2,394	370	15.4
All groups	8,124	845	10.3

TABLE 2.—*Classification of Positive Brucellergin Reactors Based on Opsonic Tests*

	Number	Percentage
Infected	623	73.7
Immune	222	26.3
Total	845	100.0

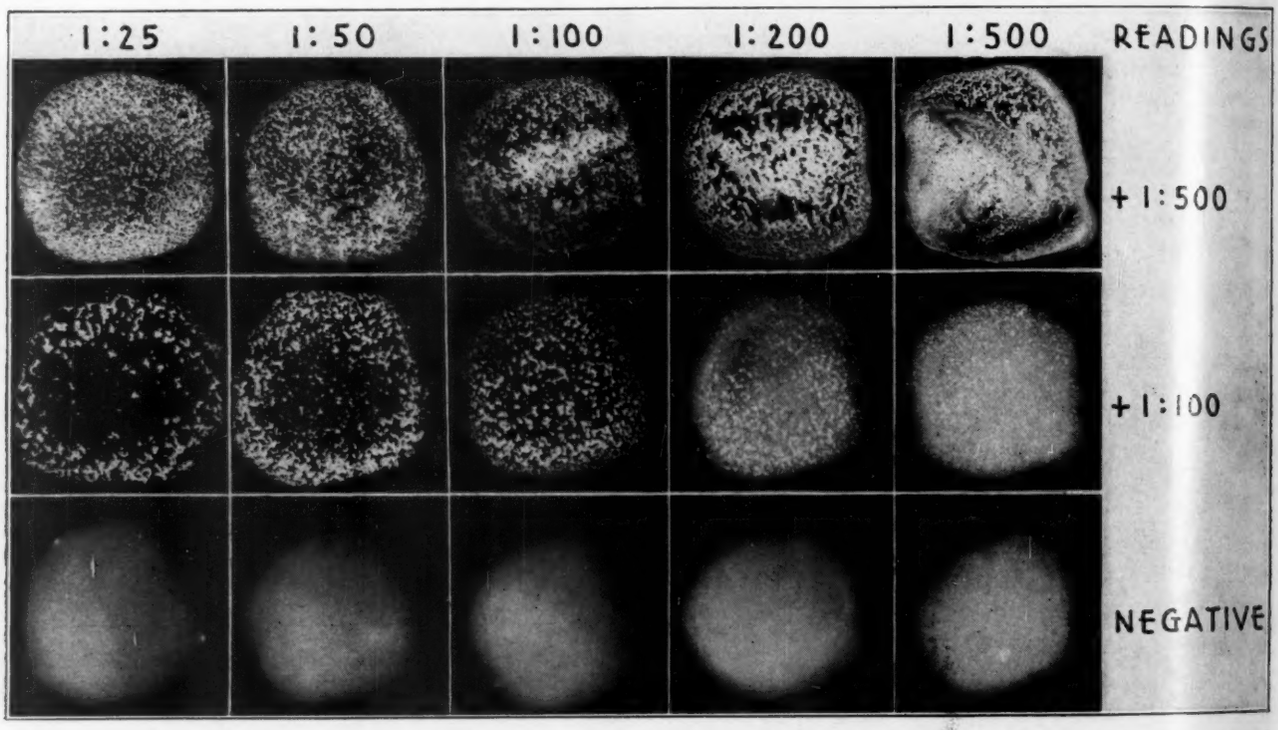


Fig. 3.—Rapid agglutination test. Note complete agglutination in serum dilutions of 1:500 and 1:100.

3. A negative agglutination test does not rule out brucellosis. A positive agglutination test consists of complete agglutination in a titer of over 1:25.

4. A positive culture may be found for active infection or for carriers of the disease.

RESULTS OF SURVEY AT ELOISE HOSPITAL

An unusual opportunity to study the incidence of Brucella infection presented itself at Eloise Hospital and Infirmary, whose milk supply was partly infected with Brucella. This public institution of Wayne County (in which the city of Detroit is located) has three divisions: a general hospital (William J. Seymour Hospital), an infirmary for homeless indigents and a mental hospital. All persons in the institution were first tested intradermally with brucellergin.

Table 1 shows the number and percentage of positive reactions among the following groups: hospitalized patients, indigent persons, indigent food handlers, employees and mental patients. Among 8,124 persons tested, 845, or 10.3 per cent, showed positive brucel-

2. Recently a new and superior medium called Bacto-Tryptose agar (Difco) has been developed for the isolation of Brucella in the laboratories of Michigan State College.

lergin reactions. The incidence roughly paralleled the average length of stay of the various groups in the institution. The incidence was lowest among the hospitalized group (6.2 per cent), whose average stay was the shortest, and greatest among the mental patients (15.4 per cent), whose average stay was the longest.

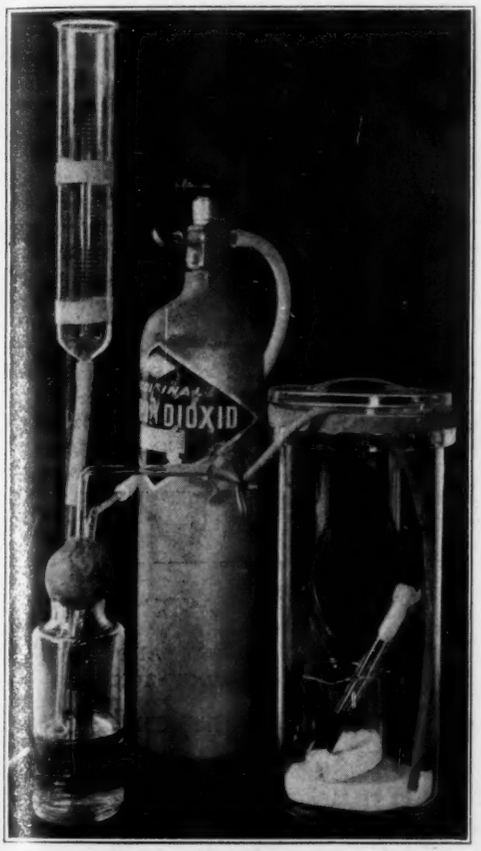


Fig. 4.—Apparatus used to produce a 10 per cent carbon dioxide atmosphere for culture of Brucella.

The 845 persons with positive brucellergin reactions were then classified by means of the Brucella opsonic test as infected or immune. In 623, or 73.7 per cent the polymorphonuclear leukocytes showed absent, slight

TABLE 3.—*Classification of Infected and Immune Persons According to Sex*

	Intradermal Tests	Positive		Infected		Immune	
		Number	Percentage	Number	Percentage	Number	Percentage
Male	5,801	528	9.1	422	7.3	106	1.8
Female	2,323	317	13.6	201	8.6	116	5.0
Total	8,124	845	10.3	623	7.7	222	2.7

or moderate phagocytosis of Brucella organisms, and the individuals were classified as infected. The remaining 222, or 26.3 per cent, showed marked opsonic power and were classified as immune (tables 2 and 3).

Seven hundred and twenty-five persons with negative brucellergin reactions were tested by means of the rapid agglutination method. Only one showed a significant serum agglutination titer (over 1:25). Among 845 subjects with positive brucellergin tests, 111, or 13.1 per cent, showed a significant serum agglutination titer (table 4). Of the 623 infected persons, thirty-three, or 5.3 per cent, gave a positive agglutination test. Of the 222 immune persons, seventy-eight, or 39.6 per cent, gave positive agglutination tests (table 5).

The positive brucellergin reactions were accurately measured in all cases and were classified into three groups, as follows: those measuring from 0.5 to 2.5 cm. in diameter, those measuring from 2.5 to 7.5 cm. in diameter and those measuring over 7.5 cm. in diameter. The size of the intradermal reactions showed little or no relation to the status of Brucella infection or immunity (table 6). The percentage of reactions over 7.5 cm. in diameter was only slightly greater among the immune persons (30.2 per cent) than among those infected (22 per cent).

TABLE 4.—*Comparison of Brucellergin and Agglutination Tests*

Reaction	Brucellergin	Agglutination	Percentage Agreement
Negative	725	724	99.9
Positive	845	111	13.1

TABLE 5.—*Agglutination Titer in Brucella Infected and Immune Groups*

Group	Number	0 to 1:25	1:50	1:100	1:500	Over 1:25 Number	Over 1:25 Percentage
Infected	623	590	11	13	9	33	5.3
Immune	222	144	42	24	12	78	39.6
Positive brucellergin reaction	845	734	53	37	21	111	13.1

Cultures of the blood were made for all 845 individuals with positive brucellergin reaction and of the urine for 370 infected persons. The Brucella organism was isolated from the blood in four instances of active infection: Brucella abortus once and Brucella suis three times. In addition, Brucella suis was isolated from the urine of one carrier and from the urine and the

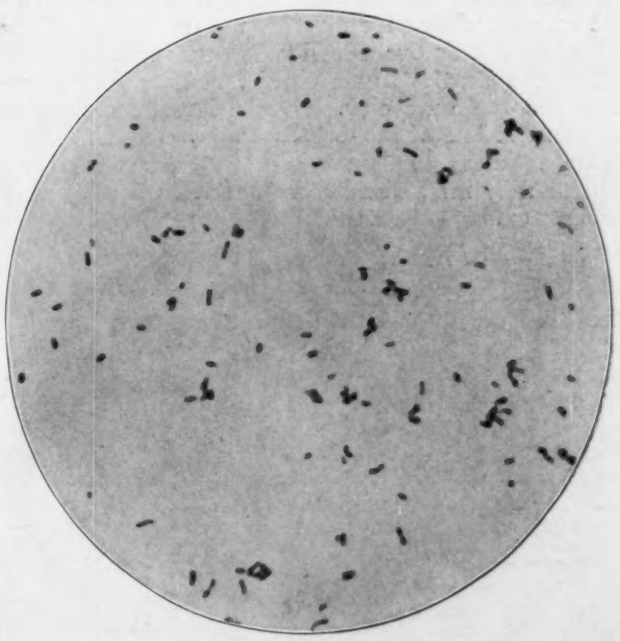


Fig. 5.—Brucella abortus; × 1,800.

stool of a second carrier. The Brucella suis infections were probably not contracted through the milk used in the institution.

The brucellergin, opsonic and agglutination tests were repeated after five months on ninety-nine persons with negative tests, 103 infected persons and eighty-four immune persons. The comparison of the Brucella status of the subjects in these groups after the five

months interval is shown in table 7. The size of the brucellergin reactions and the results of the opsonic and agglutination tests showed remarkably close similarity to those of the first tests.

The milk used in the institution was unpasteurized and was obtained partly from a milking herd of eighty-five cows, nine of which were found to be eliminating

TABLE 6.—*Size of Brucellergin Intradermal Reactions in Brucella Infected and Immune Groups*

Group	Number	0.5 to 2.5 Cm.		2.5 to 7.5 Cm.		Over 7.5 Cm.	
		Number	Percentage	Number	Percentage	Number	Percentage
Infected	623	196	31.5	290	46.5	137	22.0
Immune	222	45	20.3	110	49.5	67	30.2
Total reactions	845	241	28.5	400	47.3	204	24.2

Brucella abortus in their milk, and partly from five other herds whose milk was free from Brucella abortus. The incidence of infection among the various hospital groups as judged by the intradermal tests appeared to vary in proportion with the average length of stay in the institution. Table 4 shows clearly that the brucellergin reaction is much more sensitive than the agglutination test in the detection of Brucella infections and that the agglutination test is positive in only a small percentage of cases of infection. It would therefore seem that the agglutination test should be used as a confirmatory test rather than be relied on for diagnosis. While a positive agglutination test is of definite value, a negative agglutination test cannot be considered to rule out the presence of brucellosis.

The results of the check of the various tests after five months among the groups of negative reactors, infected subjects and immune persons showed remarkable correspondence for most of the methods. Of the ninety-nine negative reactors (forty-six males and fifty-three females), nine females had a positive reaction and five were classified as infected and four as immune. None of the males were infected. This was taken to mean that the new infections were being produced by infected milk or more likely by means of carriers among the women.

SUMMARY

1. The brucellergin test is the most sensitive test in the diagnosis of brucellosis. If the test is negative, brucellosis will usually be ruled out.

TABLE 7.—*Results of Brucellergin and Opsonic Tests on Negative Reactors and Infected and Immune Persons After Five Months*

Original Classification		Classification Five Months Later		
	Number	Negative	Infected	Immune
Negative	99	90	5	4
Infected	103	3	69	33
Immune	84	0	4	80

2. If the test is positive, the opsonic test should then be performed to determine whether infection or immunity is present.

3. A negative agglutination test does not rule out Brucella infection. The agglutination test is diagnostic only in a small percentage of cases and gives no information as to the immune status of the subject.

4. Carriers of Brucella may be of some importance in the spread of the disease.

ABSTRACT OF DISCUSSION

DR. I. FOREST HUDDLESON, East Lansing, Mich.: After hearing the results of the survey at the Eloise Hospital as presented by Dr. Gould, the question arises as to whether we were justified in classifying such a large number of individuals showing positive allergic reactions as infected. The classification is based on published and unpublished data which have been obtained in cases of undulant fever that yielded positive cultures from the blood, stools or urine. We shall continue to adhere to this classification until some one following the same technic shows that the classification is erroneous. The usefulness of this system of tests will depend on how they are performed and interpreted. In the case of the intradermal test with brucellergin, the time interval of reading the test is important. If the result of the test is read under forty-eight hours it is likely to be misinterpreted, as about 50 per cent of nonallergic individuals show an intense erythematous reaction at the twenty-fourth hour. Such a reaction may be mistaken for a specific one. The accuracy of the results of the phagocytic test will depend on the adherence to the prescribed technic. The selection of the proper culture for the test is highly important. Certain strains are phagocytized by cells in normal blood as well as in immune blood. The type of reagents and concentration of the reagents used in making the test should be selected very carefully. We do not wish to take the position that the phagocytic test or allergic test cannot be improved. Before one attempts to change the system of tests for diagnosing undulant fever, it is hoped that a large number of comparative tests will be made before the present system is discarded.

PULMONARY ASBESTOSIS

IV. THE ASBESTOS BODY AND SIMILAR OBJECTS IN THE LUNG

KENNETH M. LYNCH, M.D.

CHARLESTON, S. C.

One of the conspicuous and interesting features of the pulmonary condition resulting from the inhalation of asbestos dust by miners and mill workers in this material is the occurrence of certain curious bodies in the lungs and peribronchial lymph nodes and frequently in the sputum.

These objects have been sufficiently described,[1] but it is relevant here to review briefly their characteristics. They measure from about 10 to more than 100 microns in length and from about 1 to 12 microns in thickness and are composed of a central translucent fiber or needle crystal, the asbestos crystal, with an enveloping shiny golden or brownish substance constructing various architectural figures. The whole object may be a rod with smooth blunt ends or, more often, with one or both extremities in a single rounded knob or a clump of such knobs, reminding one of the fruit body of Aspergillus. Frequently the shaft is a series of rounded beads or disks strung closely along the central filament. Again the object may be of the shape of a club, often with one knobbed end, or it may be a long slender filament. Spherical forms of various sizes are also seen. Characteristically these bodies give a prussian blue reaction for iron.

McDonald [1] advanced the hypothesis that the asbestos body is a particle of asbestos fiber in the process of alteration and absorption by hydrolysis, with the silica passing into a colloidal state and a gel.

From the Department of Pathology, Medical College of the State of South Carolina.

Read before the Section on Pathology and Physiology at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 11, 1937.

1. McDonald, Stuart: Histology of Pulmonary Asbestosis, Brit. M. J. **2**: 1025 (Dec. 3) 1927. Lynch, K. M., and Smith, W. A.: Asbestosis Bodies in Sputum and Lung, J. A. M. A. **95**: 659 (Aug. 30) 1930.

IN THE LUNGS

These bodies may be found in the lungs of asbestos workers, within the bronchioles, the alveoli near about and the interlobular, peribronchial and subpleural tissues along the lymphatic route. They occur also in peribronchial lymph nodes, within sinus walls and

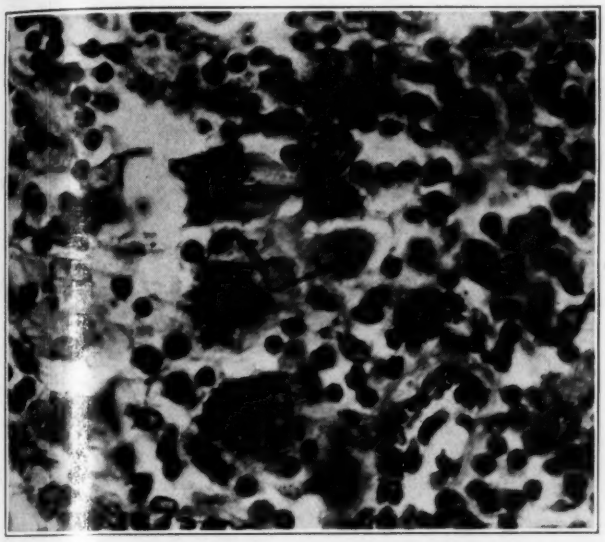


Fig. 1.—Asbestos bodies in peribronchial lymph node; reduced from a photomicrograph with a magnification of 1,000 diameters.

embedded in fibrosed areas. Here they are usually of the shorter lengths, although some may be surprisingly long considering their route of collection through small lymphatic channels. I have seen them within veins in the lungs, where they may have been dragged in the course of sectioning the tissue, and at least one typical form was found embedded in the splenic pulp. Stewart, Bucher and Coleman [2] have reported finding them also in the spleen.

Characteristically they are limited to the bronchial tract, the adjacent pulmonary alveoli, the peribronchial connective tissues and the peribronchial lymph nodes.

EFFECTS

In the alveoli they are usually associated with or enclosed by phagocytes, mononuclear or multinuclear, some large foreign body giant cells occurring massed about those of large size. This may be the only cellular reaction to their presence. The following case illustrates this fact:

CASE 1.—A Negro, aged 35, whose death was due to arteriosclerosis and pontine hemorrhage, had worked in the carding room of an asbestos factory for a total of five years during an elapsed period of seven years, beginning fifteen years before his death. During his exposure there was no adequate system of dust disposal in this plant; in fact, it was before the recognition of a potential hazard in the industry and the institution of measures of protection of the workers from the dust.

In spite of an undoubtedly heavy exposure and the length of time during which the bodies remained in the lungs, and although they had become deposited within the interlobular tissue around bronchioles, there was no definite fibrosis or other reaction to them, only phagocytosis of those remaining in alveoli. The lung generally was normal on gross and histologic examination except for an old puckered scar of the left apex.

It appears, therefore, that the presence of this material in abundance and over a long period does not necessarily result in fibrosis or other apparent damage to the tissue. That is to say, the anatomic disease asbestosis may not be assumed to exist simply because of quantity exposure of such a duration, an assumption apt to be the case under current conception.

Often, however, the asbestos bodies not only incite phagocytosis while within bronchioles and particularly alveoli but enter the tissues and apparently the lymphatics and lodge along the course, tending to stimulate growth of fibrous tissue about them. Thus fibrosis of the course of lymphatic circulation in the lungs and peribronchial lymph nodes is the resulting disease. It is generally accepted by students of the condition that the disease is a diffuse type of fibrosis rather than the nodular form of silicosis proper. Lynch and Smith [3] have already reported, however, on the occurrence of nodular fibrosis from asbestos inhalation, and I expect to consider this matter again in a separate report.

IN THE SPUTUM

In addition to the conspicuous presence of asbestos bodies in the area of the lung at autopsy, they may be found in the sputum of asbestos workers, by direct microscopic examination of the wet preparation when in numbers or in the sediment of a strongly alkaline solution of sodium hypochlorite or 10 per cent sodium hydrate-digested sputum, even when few.

According to my experience, the presence of these objects in the sputum indicates only inhalation of asbestos dust of sufficient duration for them to be formed. It is apparently possible to find them under conditions probably not conducive to disease. On the other hand, they may not be found even when the lungs are extremely disabled by fibrosis and the bodies are within the bronchioles and alveoli in large numbers.

Fig. 2.—Deteriorating asbestos bodies in a case of asbesto-silicosis; reduced from a photomicrograph with a magnification of 1,000 diameters.

I have found them in the sputum of an engine room worker at an asbestos plant whose exposure to the dust was not material and who exhibited no evidence of pulmonary abnormality. On the other hand, in three

2. Stewart, H. L.; Bucher, C. J., and Coleman, E. H.: Asbestosis: Report of Two Cases, Arch. Path. **12**: 909 (Dec.) 1931.

3. Lynch, K. M., and Smith, W. A.: Pulmonary Asbestosis: II. Including the Report of a Pure Case, Am. Rev. Tuberc. **23**: 643 (June) 1931; Pulmonary Asbestosis: III. Carcinoma of Lung in Asbesto-Silicosis, Am. J. Cancer **24**: 56 (May) 1935.

cases of long standing extreme fibrosis of the lung, in which many bodies were observed in the lung at autopsy, they failed to appear in examinations by the concentration method of a number of specimens of sputum. Apparently in the fixed state of the lung, with dilatation of bronchioles and alveoli, in extreme fibrosis, these bodies may not be expelled to the exterior.

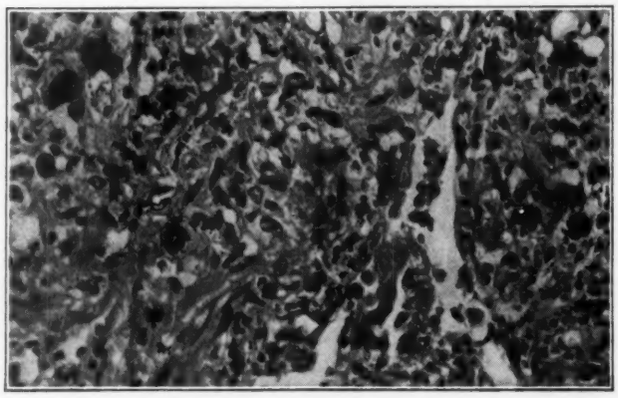


Fig. 3 (case 4).—Asbestos-like bodies in lung of cotton compress worker; reduced from a photomicrograph with a magnification of 860 diameters.

Their presence in numbers in sputum indicates material exposure at a comparatively recent time but without sufficient disability to interfere with the normal course of expulsion of dusts. It does not indicate a grade of asbestosis proportionate to the numbers of the bodies. That is to say, their absence from the sputum of asbestos workers may be consistent with advanced asbestosis, while their presence does not necessarily mean actual pulmonary damage.

ALTERATION

How long these bodies may remain intact and of characteristic form and color within phagocytes and

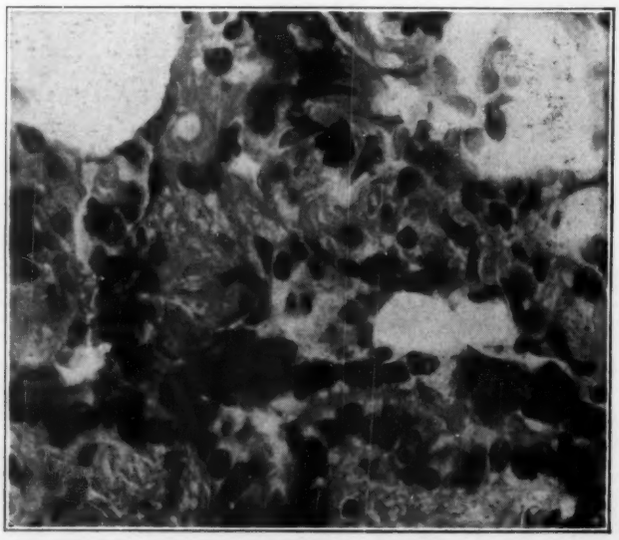


Fig. 4.—Asbestos-like bodies in lung; reduced from a photomicrograph with a magnification of 860 diameters.

within living cellular tissues is unknown. Their tenure of residence is long and may be looked on as practically permanent, from their preservation after many years. However, it appears that they may undergo the changes of dissolution and may possibly disappear. In fact, the beaded forms are looked on by some authorities as "weathered" forms.

Besides such changes, which may indicate deterioration, there occur in old deposits bodies of similar form, usually of the smaller clubbed types but not of the characteristic golden or brown color. Instead they take the hematoxylin in routine hematoxylin and eosin staining of microscopic sections. I have seen these forms in fair numbers within old hyaline fibrous areas in association with typical brown bodies in surrounding tissues. These bodies must have been in situ for a long time. Further, I have encountered like hematoxylin-staining bodies within old caseous areas of tuberculosis associated with asbestosis. I take these bodies, on the basis of their morphology, to be altered asbestos bodies, not only changed in substance but also decreased in size. As to the question of their disintegration, in the depths of some old fibrous areas and within some old necrotic associated tuberculous lesions I have failed to find any, although to judge by their numbers in similar locations elsewhere they must have been present at some time.

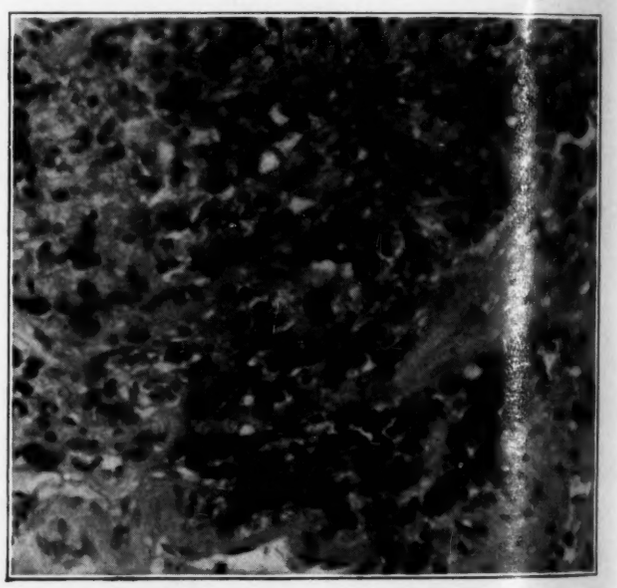


Fig. 5.—Asbestos-like bodies in lung, in dust deposit, in a patient with heart failure; reduced from a photomicrograph with a magnification of 475 diameters.

OTHER DUST BODIES

After the discovery of the asbestos body the presence of such brownish objects within the lung came to signify practically a previous exposure to asbestos dust. This idea has been altered by the finding of similar bodies when no such exposure had occurred. Tylecote and Dunn,[4] Cooke[5] and others have called attention to the occurrence of dust particles with brown coating in the lungs of workers in coal.

I have observed a considerable number of autopsies, following death from a variety of diseases, in which the lungs contained brown bodies to be compared to asbestos bodies. The following cases are illustrative:

CASE 2.—A Negro, aged 32, who had been a coal shute worker most of his working life and had not worked in asbestos at any time, died of chronic pulmonary and adrenal tuberculosis. In his lungs, besides large deposits of black granular and splinter material in fibrosed areas about interlobular vessels and within giant phagocytes in certain alveoli, many brown bodies not unlike the smaller forms of asbestos

4. Tylecote, F. E., and Dunn, J. S.: Case of Asbestosis-Like Bodies in the Lungs of a Coal Miner Who Had Never Worked in Asbestos, Lancet **2**: 632 (Sept. 19) 1931.

5. Cooke, W. E.: Silico-Anthracosis Presenting Curious Bodies Similar to Those in Asbestosis, Brit. M. J. **1**: 656 (April 9) 1932.

bodies were observed. These were single spherical forms, globular and disk-shaped forms in rows or chains and club-shaped bodies and rods, some with one or both ends knobbed. Often the centrum could be made out as a black granule or, in the larger bodies, a black splinter, but the brown coating was like that of the asbestos body.

CASE 3.—A Negro housemaid, who had never worked in asbestos, died of malignant myoma of the uterus. Her lungs

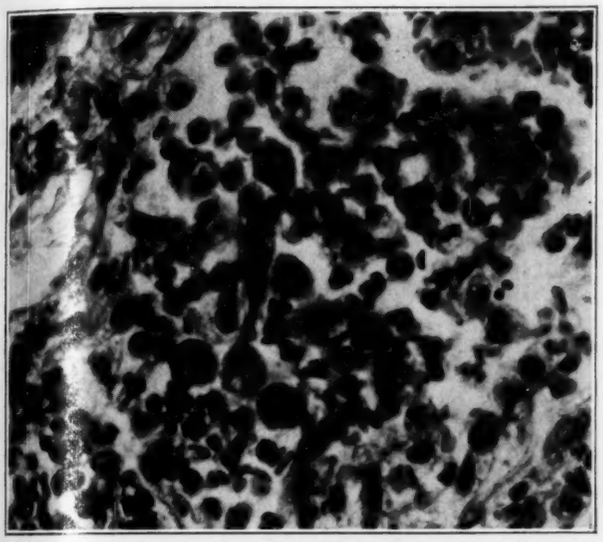


Fig. 6. Asbestos-like bodies in lung; reduced from a photomicrograph with a magnification of 860 diameters.

contained a black amorphous material, similar to that in the lungs of the coal shute worker, although less in quantity, and numerous brown bodies of like kind and of similar distribution, associated with a state of emphysema and chronic bronchitis but with no definite related fibrosis.

CASE 4.—A Negro, aged 45, who had worked virtually all his working life (20 years or more) in a cotton compress and not at all in asbestos, died of arteriosclerosis and pontine hemorrhage. His lungs contained large numbers of golden brown bodies, some closely resembling asbestos bodies. They were of the smaller sizes and of various shapes, as in the previous cases cited, and were accompanied by black dust. They did not show the black centrum but rather a central body of translucent appearance, fiber-like. In the alveoli there were large numbers of mononuclear phagocytes containing fine dust but no brown bodies. No material fibrosis was associated with the deposits.

Similar brown bodies have been observed in the lungs of a considerable number of subjects who died of heart failure, particularly rheumatism (fig. 5) and arteriosclerosis (fig. 6).

Generally the number of bodies found was small, but in some instances they were quite conspicuous. In fact, in some cases a diagnosis of asbestosis was made on routine examination and stood until investigation satisfactorily showed no such occupational exposure.

It has come definitely to my mind that chronic congestion of the lungs may play a part in the formation of some of these bodies, at least that congestion may augment or favor the formation of the enveloping substance. In this connection, a close study of the brown iron-bearing granules in the mononuclear cells in alveoli in cases of congestive heart failure (heart failure cells) will disclose that many of them contain a black granule centrum.

The bodies here described have generally been more conspicuous in cases of rheumatic heart disease. They have always been associated with black particulate matter, and except in the case of the cotton compress worker a black centrum could be seen. Only the small round forms occurred commonly in phagocytes in alveoli. The larger forms, rods, clubs and chains, were found mainly within the tissues of the interlobular framework. They gave the prussian blue reaction for iron, as does the asbestos body. Their iron content and their seeming common connection with pulmonary congestion and the local liberation of blood iron again raises the question as to whether the iron of the asbestos body may not be so related, at least in part, and whether congestion may at least favor the production of all such bodies.

In connection with this question it may be recalled that the asbestos body does not always form when asbestos dust comes to lie in the lungs or in other tissue even for periods usually sufficient to produce it. Schuster [6] reported on the occurrence of asbestosis in a dog, in which only naked asbestos fiber was found, with no brown envelop produced, while Gardner and Cummings [7] found that the asbestos fiber remained uncoated in experimental asbestosis of the rabbit.

Usually, I am confident, such deposits in the lungs may be distinguished from asbestos bodies, particularly because of the larger sizes and the translucent needle centrum of the latter, but the form is often similar and the formation of the brown smooth coating must be by the same or a similar process

SILICA BODIES

The state of the dust particles to be found in cases of silicosis proper seems to warrant special consideration in a study of the deposits associated with dust disease. In my series silicosis is scant and therefore my observation not extensive. However, in this small amount of material, including a case of advanced typical nodular fibrosis attending extreme accumulation of dust in the lung, with much deposit of hemosiderin,

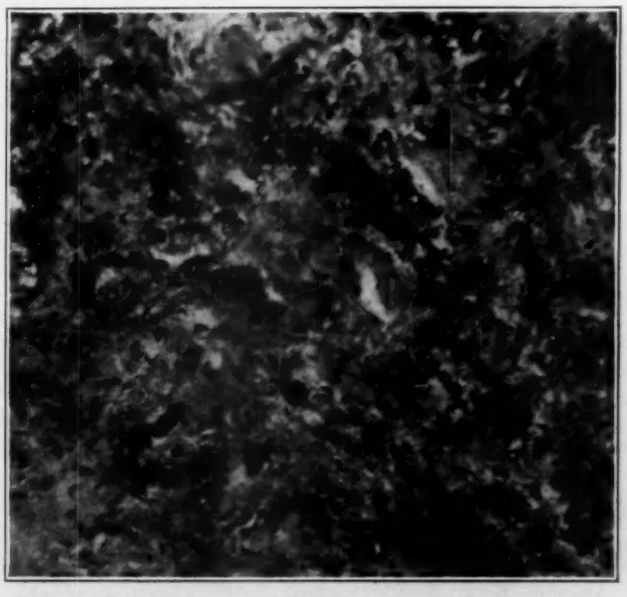


Fig. 7.—Silica bodies resembling asbestos bodies; reduced from a photomicrograph with a magnification of 375 diameters.

the formation of an enveloping substance about the dust particles similar in color and appearance to that about asbestos and the other particulate matter here discussed was striking.

6. Schuster, N. H.: Pulmonary Asbestosis in a Dog, J. Path. & Bact. **34**: 751 (Nov.) 1931.
7. Gardner, L. U., and Cummings, D. E.: Studies on Experimental Pneumonokoniosis: VI. Inhalation of Asbestos Dust; Its Effect upon Primary Tuberculous Infection, J. Indust. Hyg. **13**: 65 (Feb.) 1931.

This formation is encountered wherever the dust is found, in alveoli, associated particularly with hemosiderin granules and occurring in mononuclear phagocytes, in the interlobular tissues and in the hyaline fibrous nodules. The form of the body is dependent on the size and the shape of the dust particle of course, and none of the large bodies occurring in asbestosis are to be seen. However, the small forms seen in asbestosis are well simulated. The enveloping substance is shiny, usually less noticeable than that of the asbestos body and a lighter golden as a rule but sometimes a comparable brown.

The most common body is rounded, sometimes truly spherical, with a pale golden envelop on a black granule. When the dust particle is elongated the whole body is shaped like a rod, club or needle. Some bodies are rough and irregular, when the centrum of the dust particle is irregular, rhomboidal or chipped, but the surface of the envelop is always smooth.

The formation of these silica bodies in true silicosis seems to be just as much a part of the process concerned as in the probably related state of asbestosis.

It appears possible that other fiber or crystalline dusts not yet particularly studied may produce similar bodies and also that confusion of some consequence may result from failure to realize that asbestos bodies may be simulated by other deposits in the lung.

As to the nature of all of these objects, it appears that they are formed on a silica base, as is the asbestos body. On that hypothesis the group would become silica bodies, of which the asbestos body is a member.

16 Lucas Street.

ABSTRACT OF DISCUSSION

Dr. Henry C. Sweany, Chicago: The asbestos fiber is from 100 to 200 microns in length on an average with occasional shorter pieces. Owing to its length it has great difficulty in following the lymphatic channels. It is usually stopped in the smaller bronchioles and from there works its way through the bronchial wall and but rarely proceeds much farther. Therefore there is not the tendency to enlargement of the hilar lymph nodes seen in silicosis. The fibrosis has a tendency to be more of a linear and stringy type and does not tend to form into the regular "ball of twine" whorls seen in silicosis. One of the similarities between silicosis and asbestosis is the individual difference that Dr. Lynch has mentioned between one patient and another. The disease may develop in one person much more readily than in another, yet some may be exposed for a long number of years without showing much detriment. It is a most important and timely observation relative to the presence or absence of these asbestos bodies. He has pointed out wisely that sometimes they may be present when the patient has no asbestosis and that they may be absent with an asbestosis. It isn't so simple as to take a little sputum, make a smear and find these golden yellow bodies. It is really quite difficult to establish a definite diagnosis of the disease. I should like to ask Dr. Lynch whether he has made any observations on the character of this yellow pigment. The latest reports that I have read on the subject by Gardner, Gloyne, Bürger and Merewether say that the presence of the golden yellow pigment is thought to be due more than anything else to the presence of iron in the fibers. Asbestos is an alkali, magnesium silicate, with some calcium and some iron in various proportions, but the presence of iron seems necessary in order to give the golden color. The disintegration process that goes on causes the fibers to assume the various club shapes and ultimately they are entirely resorbed and disappear, as Dr. Lynch has shown. I believe that silicosis, in which there is pure silicon dioxide, is different. I don't recall having seen any of these golden yellow bodies in silicosis, and I have examined a large number of specimens. I believe that the iron or some other substance in the asbestos fiber is more responsible for the color and therefore one should not expect to find it in silicosis. It is pertinent that these old chronic cases with passive congestion and accumulation of iron may also show golden yellow bodies, as I have seen them in other diseases.

Dr. Kenneth M. Lynch, Charleston, S. C.: In reference to the occurrence of objects in the spleen which may be mistaken for these bodies, they have been reported in that location. I have seen there in a few cases objects that I wanted to call asbestos bodies, but I really did not know whether they might be other bodies coated with iron in the congested state of the spleen. I presume that the iron has something to do with the formation of this smooth brown coat about the asbestos fiber in the lung. However, it doesn't always form. In the lungs of a rabbit in experimental asbestosis, Gardner observed that the asbestos fiber remained naked and did not become coated with this brown material. Shuster has reported that in asbestosis in a dog the fiber was naked, without any coating. So far as I know, the material is considered a colloid developed from decomposition of the silicate, the asbestos fiber, by a process of hydrolysis, probably at the beginning of deterioration and decomposition of the material, in connection with the living tissue. I cannot say much about the occurrence of smaller objects of similar kind in silicosis because I see very little silicosis. I think we have got to break down pneumoconiosis into consideration of the effects of special kinds of dusts, that is, the material making up the dust, rather than considering silicosis as a whole. It is not unlikely that there are other dusts that have not yet been studied which may come in for some part in pneumoconiosis. I have studied the dust of fertilizer factories, in the lungs of workers, without discovering any change in the dust at all, or any influence on the lung. Dr. Sweany is correct about the opportunity for collection of these larger objects through the lymphatic circulation of the lung as compared to the smaller granules of silicosis. They collect more along the bronchial route, that is, around the bronchi, but they do occur in the lymph nodes of the hilus to a surprising extent. When one considers the size of them and how those rather angular particles must be transported through the lymphatics to arrive finally in the numbers I have seen in some lymph nodes, it is astonishing. I believe, however, that more of the deteriorated forms are seen in lymph nodes than in the lung tissue.

Clinical Notes, Suggestions and New Instruments

BURNS FROM IGNITION OF CELLULOID COMBS

Howard Fox, M.D., New York

The danger of severe burns from ignition of celluloid combs is not generally recognized by the public. Such burns have usually occurred while the so-called water wave was being made in the hair. In this beautifying process the scalp is first shampooed or simply moistened, the combs are placed in suitable position and the hair is then allowed to dry by room temperature or by artificial heat. It is during the drying process by artificial heat that disastrous results may take place if the heating apparatus is too close to the hair.

Six cases of severe burns from the ignition of celluloid combs have come to my attention in the last few years. In all of them the scalp was injured by third degree burns, causing scars and permanent loss of hair. All except one of these patients also had burns on other parts of the body. Two of them were severely injured when the clothing was set on fire.

In one of these cases the accident occurred in a beauty parlor, in the others when the victims were at home. The source of heat used for drying the hair in these cases was either an electric lamp, a gas heater or a stove.

REPORT OF CASES

Case 1 (Oct. 14, 1927).—Mrs. M., aged 40, while visiting friends in a German city, attempted to produce a water wave, using twenty or more celluloid combs which she had brought from the United States. She then dried her hair near a porcelain stove. Ignition of the combs produced a third degree burn of almost the entire vertex and upper occipital region. The burns healed in ten weeks. When seen in consultation

after the lesions had healed, the affected part of the scalp was red, atrophic and bald. There was also some scarring of the left side of the forehead and left ear as a result of the burns.

CASE 2 (Oct. 17, 1927).—Miss O., aged 32, while having a water wave at a beauty parlor suffered a third degree burn, 3 by 4 inches (7.6 by 10 cm.) on the parieto-occipital region. One or more of the combs ignited from the heat of a large lamp. On putting her hand to her scalp she also sustained second degree burns of her palm and fingers. The lesion of the scalp was healing at the end of three weeks when the patient was last seen.

CASE 3 (March 31, 1930).—Miss P., aged 25, while giving herself a water wave three years previously, used four celluloid combs. In drying her hair she sat in front of a gas heater. The combs ignited and the flames were extinguished by her mother, who threw a blanket over the patient's head. The burned area required four months to heal. At the time of examination she presented a completely bald atrophic area about 2 inches in circumference on the frontoparietal region.

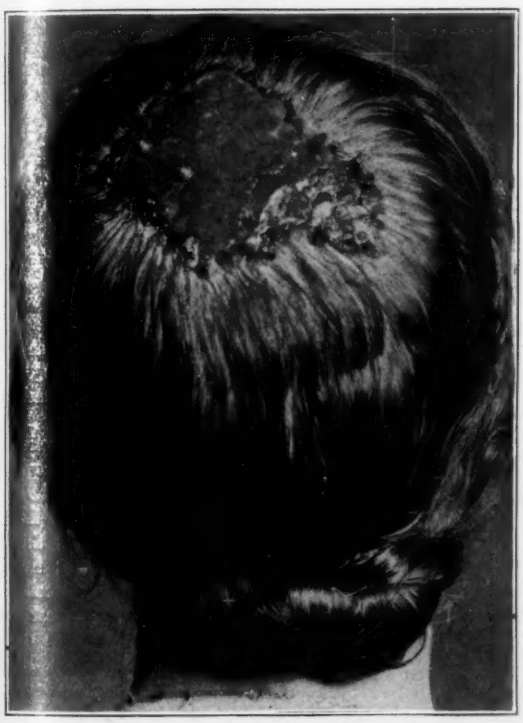


Fig. 1 (case 2).—Third degree burns of scalp.

CASE 4 (July 17, 1931).—Miss X., aged 18, while waving her hair in December 1929 used six celluloid combs and dried the hair with a small electric hand lamp. As a result of ignition of the combs and clothing she sustained burns of the scalp, face, ears, neck and both shoulders and right hand. The burns varied from second to third degree and required subsequent skin grafting on the scalp, face and shoulders. As a result of her injury she was confined to bed at home and in a hospital for three months. Examination showed several bald atrophic areas of the scalp, the largest being 2½ inches (6.3 Kg.) in the longest dimension. There was some loss of tissue of the right helix, forehead, nose, upper part of the cheek and right eyebrow. There were also slightly elevated scars on the shoulder and smooth scars on the neck, on the supraclavicular region and on several fingers.

CASE 5 (July 15, 1931).—Miss H., aged 18, while waving her hair with celluloid combs in August 1930 used an electric lamp for drying purposes. The combs ignited, burning her clothing and producing severe burns which confined her to bed for six weeks. Examination showed four areas of baldness and scarring in the left parietal region, the largest area being 1½ inches in length. There were also keloidal scars in the right axilla, the mastoid and supraclavicular regions and the right elbow.

CASE 6 (June 24, 1936).—Miss M. D., aged 22, a patient of Dr. Maurice J. Costello, gave herself a water wave Oct. 10, 1935, with twelve celluloid combs. While using a heat lamp for drying the hair she heard an explosive sound, followed by burning of her hair and some of her clothing. She sustained third degree burns of the scalp, hands and left knee, which required hospitalization for two months. Some of the burns did not heal completely until the end of one year. She now presents an area of permanent baldness the size of a palm and scarring in the right parietal region. There is a smaller scar on the right side of the forehead and there are also scars on the hand and right knee. When performing the water wave, the patient thought she was using "india rubber" combs. However, they burned suddenly in an explosive manner, and one of them, submitted later to Dr. Costello, proved to be made of celluloid and not of rubber.

Fig. 2 (case 5).—Scars from burns due to ignition of celluloid combs and clothing. The patient was confined to bed for six weeks.

COMMENT

Combs for the production of water waves are frequently made of celluloid and apparently owe their popularity to the fact that they are light in weight, flexible and cheap. They are sold in large numbers at some department stores and at practically all five and ten cent stores. All celluloid combs are extremely dangerous to use in the hair if artificial heat is applied for drying purposes. Celluloid combs burn almost instantaneously and noiselessly and set fire to the hair before the victim realizes what has happened.

Fig. 3 (case 6).—Scar from burn of scalp, which required a year to heal. The patient remained in the hospital for two months.

Samples of different varieties of combs for making water waves were obtained from twenty different stores in the metropolitan district of New York. The majority of the combs were made of celluloid, some were made of hard rubber and a few were of metal.

Metal combs are naturally safe but they are not widely used, probably because they are rather heavy and stiff and tend to scratch the scalp. Hard rubber combs are more popular, though most of them are inflammable. They are, however, somewhat less dangerous than celluloid combs, since they do not burn as rapidly and they are apt to give a crackling sound of warning on ignition. One type of comb was advertised as being "noninflammable." This did not prove to be true, as a sample that was purchased burned readily. This was a metal comb coated with lacquer.

A warning of the danger of ignition of inflammable combs is often given the purchaser, but it is apparently seldom heeded. Captions such as "inflammable, avoid heat" and the like are often printed on the carton containing the combs for sale or in some cases are stamped on the individual comb. On some there is no warning whatever. On two occasions the saleswoman stated that certain combs were not at all inflammable, though when tested later they burned almost instantaneously when a match was applied to them.

It is hard to understand why a manufacturer or seller of a dangerous article such as celluloid combs should not at least protect himself against possible litigation by suitable warning of fire hazards. My contention is however that, even though such a warning is given regarding the inflammability of celluloid combs, they should never be allowed to come in close contact with heat.

SUMMARY AND CONCLUSIONS

1. Six cases of third degree burns followed ignition of celluloid combs, which were used by women for producing "water waves."

2. Celluloid combs should never be used when heat is applied to dry the hair.

140 East Fifty-Fourth Street.

"PLEURAL ASCITES": THE RESULT OF TRAUMATIC RUPTURE OF THE DIAPHRAGM IN A CASE OF LATENT HEPATIC CIRRHOSIS

SAMUEL GOODMAN, M.D., TULSA, OKLA.

A careful search of the literature on traumatic rupture of the diaphragm, of which there are well over 1,000 cases recorded, fails to show one similar to the following case. The unusual angles presented during the course of the patient's illness provided a most difficult problem in diagnosis.

REPORT OF CASE

History.—A man, aged 56, an oil producer, admitted to St. John's Hospital Jan. 17, 1937, complained of cough, shortness of breath, weakness and fever. Three days before admission a temperature of 103 F. developed with increasing cough and dyspnea. Dulness was found over the base of the right lung and the breath sounds over the same area were quite distant. The fever abated but the area of dulness increased during the next two days. He was referred to my service at the hospital on the following day.

The patient had been in an automobile accident Dec. 9, 1936, and was admitted to another hospital in the city with a fracture of the sternal end of the right clavicle and a fracture of the second and third ribs on the right side near the sternal junction. At that time he was in moderate shock and slightly cyanosed. He had a cough with expectoration of frothy blood and subcutaneous emphysema over the wall of the upper right side of the chest. The temperature was 100.4 F., the pulse was 80 and the respiration rate was 28 and shallow. Examination of the chest at that time showed evidence of collapse of the right lung. The white blood cell count was 10,650, polymorphonuclear leukocytes 82 per cent, lymphocytes 14 per cent, monocytes 2 per cent, eosinophils 2 per cent. The urine showed a trace of albumin, with occasional hyaline casts and a few pus cells. The Kahn reaction of the blood was negative. During his stay in the hospital the cyanosis gradually disappeared, but he continued to cough and had a temperature ranging from 98 to 100 F. He was discharged December 18. He was seen several times at his hotel room and continued to improve, although he still had slight elevations of temperature, cough and dyspnea on moderate exertion.

His past history was irrelevant except for the fact that he drank alcoholic liquors freely and that he had syphilis, which had been treated intermittently since 1929. He had had considerable antisyphilitic treatment, including a course of malarial treatment in 1931, at which time it was thought that there was some evidence of dementia paralytica. He continued, however, to carry on a successful business until the date of the accident. There was no history of gastro-intestinal symptoms or of systemic disturbances.

Examination.—The patient was fairly well nourished and developed with slight dyspnea, but apparently he was in no great discomfort. Examination relative to the head and neck was negative except that the mouth was edentulous, the tonsils were large but not septic, and there was some engorgement of the superficial veins on the right side of the neck. The chest was elliptic, the right side being larger than the left. There was a bony deformity of the right clavicle at the sternoclavicular articulation. No expansion could be detected on the right side, which was absolutely flat on percussion from the apex to the base. Breath sounds were distant throughout the entire right side of the chest. Tactile and vocal fremitus were diminished. The left lung was clear. Examination of the heart showed the point of maximum impulse at the fifth interspace in the left midaxillary line. The sounds were of good quality and the rhythm was regular. The abdomen was scaphoid. There were no masses or muscular tenderness. Some fulness and increased resistance was noted in the upper right quadrant below the costal margin. There were no dilated superficial veins. Neuromuscular examination was negative. There was no edema of the extremities. The genitourinary tract was normal except for a scar 4 mm. in diameter on the right side of the glans penis. Rectal examination was negative. The laboratory examination showed hemoglobin 80 per cent, red blood cells 4,200,000, white blood cells 3,500, neutrophils 78 per cent, lymphocytes 20 per cent, eosinophils 1 per cent, basophils 1 per cent, Cook Ponders index 1.91. The temperature was 99.6 F., pulse 80, respiration rate 22. The Wassermann and Kolmer reactions were two plus; the Kahn reaction was negative and the Kline reaction was two plus. The urine was normal except for a few white blood cells and a specific gravity of 1.030. Roentgenograms of the chest showed a marked opacity of the entire right lung field with displacement of the heart and mediastinum to the left. Jan. 18, 1937, the right side of the chest was aspirated and 3,000 cc. of a straw colored clear fluid was obtained, which had a specific gravity of 1.012 and showed but few cells and no bacteria. Culture was negative. Three days later, 2,400 cc. of the same type of fluid was aspirated. Following this aspiration a succession splash could be obtained, and there was amphoric breathing above the level of the fluid.

Radiologic examination of the chest on the following day showed pneumothorax extending to the apex from the third interspace and a marked opacity below to the base. The heart was still displaced to the left. Examination January 25 showed evidence of a reaccumulation of fluid, which increased gradually the next three days. January 28, 5,200 cc. was aspirated. January 30, 2,500 cc. of fluid was aspirated. February 1, 3,700 cc. of the same type of fluid was aspirated. Roentgenograms of the chest, February 2, showed the level of fluid at the third rib anteriorly with pneumothorax above the fluid level. February 3, the white blood cells numbered 9,650, neutrophils 88 per cent, lymphocytes 12 per cent, Cook Ponders index 2.11. February 6, the right side of the chest was again aspirated and 3,000 cc. of fluid was obtained. An examination of this fluid showed 85 per cent neutrophils, 5 per cent eosinophils and 10 per cent other types. Culture was negative. February 8, 650 cc. of the same type of fluid was aspirated. In view of the rapid refilling of the right pleural cavity with fluid it was deemed advisable to determine if possible, with injection of iodized oil, whether this rapid refilling might not be due to a bronchial fistula. A total of 20,450 cc. of fluid was aspirated during a period of twenty-one days. February

10, roentgenograms taken both in the supine and in the upright position showed no free iodized oil in the pleural cavity. It did show a marked compression of the right lung with good filling of the left bronchial tree. The upper fluid level in the right side of the chest was at the fourth rib.

Course.—During the period from the date of entrance to February 11 the patient was not unusually uncomfortable. The temperature range was from 98 to 101 F. There was moderate discomfort of the chest and some anorexia with increasing loss of weight and increasing weakness. February 12 the patient became drowsy, the skin developed an icteric tinge, the abdomen became distended, and an indefinite fluid wave could be obtained. The Wassermann reaction of the spinal fluid was negative. During the ensuing twenty-four hours the patient failed rapidly. February 13, nonprotein nitrogen was 36 mg. The icterus index could not be determined because of hemolysis. Anuria developed and he became comatose and died, apparently of acute liver failure. Autopsy was performed by Dr. I. A. Nelson two hours after death.

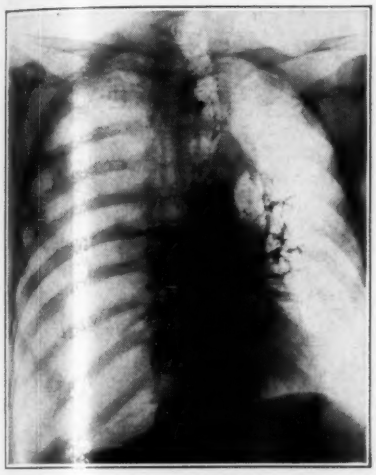


Fig. 1.—Appearance Feb. 10, 1937, on bilateral injection of iodized oil with patient in supine position. Note compression of right bronchial tree and finger-like opacity in region of right diaphragmatic sulcus. Autopsy proved this to be omentum projecting into the pleural cavity.

Autopsy.—The body was well developed but somewhat emaciated. External examination showed no jaundice in artificial light; no scars were evident. The bones were regular except for some protuberance of the right clavicle at the sternoclavicular junction. The pupils were dilated and equal.

Internal examination of the thorax showed the right pleural cavity filled with a straw colored fluid and all lobes collapsed. The right diaphragm had a perforation about 2 cm. in diameter at the dome with a portion of the omentum passing through it. The omentum was adherent to the anterior edge of the perforation but failed to close the opening. The tip of the little finger could pass through the unclosed portion. There were numerous small capillaries both on the diaphragm and on the omentum at the region of the adhesion. About 10 cm. of the omentum extended into the pleural cavity. This free portion of omentum was fanlike and when spread over the perforation tended to act as a flap valve. There was an additional valve mechanism formed when the abdominal pull on the omentum brought the smooth free edge of the perforation against the liver. Thus there was a free opening between the peritoneal and the pleural cavity but any tendency for fluids to flow from the pleural cavity into the peritoneal cavity was prevented by either or both valve actions.

The right parietal and visceral pleurae appeared fairly normal. The collapsed lobes of the right lung showed no areas of induration. The left pleura and lung showed no pathologic changes. The pericardial sac contained about 300 cc. of straw colored fluid. The heart weighed about 250 Gm. with valves, musculature and coronary arteries normal. The aorta showed a moderate degree of arteriosclerosis. The mediastinum and heart were somewhat deflected to the left but were not fixed.

Examination of the abdominal cavity showed a small amount of free fluid. The omentum was relatively small and directed over the anterior edge of the liver to the dome of the right diaphragm, where it was adherent, as already described. The liver weighed 870 Gm.; it was pale, with surfaces uniformly nodular with nodules about 1 cm. in diameter and the capsule somewhat fibrous. The cut surface of the liver was dry and fairly smooth, with traces of yellowish mottling and a slight granularity. The gallbladder was not distended. It emptied readily and did not contain any stones. The spleen weighed about 360 Gm. It was a purplish gray. The capsule was smooth, gray and somewhat thickened with a firm consistency. The cut surface was fairly dry. The peritoneum showed numerous delicate but distinct capillaries extending from the cardiac end of the stomach to the spleen. The pancreas weighed about 60 Gm. and was firm without tumors, hemorrhages or areas of softening.

The esophagus showed some varicosities. The cardiac end of the stomach showed some congestion. The pylorus appeared edematous. There was freedom from ulceration or tumors. The duodenum, jejunum, ileum, colon, sigmoid and rectum appeared normal. The adrenals did not show tumors, hemorrhages, cavitation or abnormalities.

The right kidney weighed 130 Gm. and the left kidney 120 Gm. The surfaces were smooth, the capsules stripped easily and the cortex and medulla were distinct. The pelves were moist, smooth and of a pinkish gray. The ureters showed no dilatations or abnormalities. The bladder was empty. The mucosa was velvety and the walls were regular. The prostate showed no enlargement or induration. The brain was not examined.

The anatomic changes found were (*a*) atrophic cirrhosis of the liver, (*b*) traumatic perforation of the right diaphragm, (*c*) hernia of omentum into the right pleural cavity with diaphragmatic adhesion, (*d*) right hydrothorax, (*e*) compression collapse of the right lung, (*f*) esophageal varices, (*g*) mild gastritis and (*h*) splenomegaly.

On microscopic examination (*a*) the heart muscle showed some nuclear anisocystosis and slight fibrous infiltration; (*b*) the left lung showed some recent bronchiolitis and the right lung marked atelectasis; (*c*) the kidneys showed cloudy swelling and focal hemorrhagic nephritis; (*d*) the liver showed lobular atrophy and regeneration with marked interlobular fibrosis. There were some small areas of fatty degeneration and some similar to central necrosis except that the lobular architecture did not conform to the venous distribution.

In a collection series of 1,003 cases of diaphragmatic hernia Hedblom found that 34.9 per cent were of traumatic origin.[1] About 95 per cent of the traumatic hernias occur on the left side.[2] There are several theories suggested as to the low incidence of traumatic hernias on the right side. It is thought that the liver acts as an effective protection to the right side of the diaphragm and that, owing to the structure of the right side, more resistance is offered to sudden increases in intra-abdominal pressure. As a result of the protection afforded by the liver, hernias on the right side are not as large as those which occur on the left side. About 50 per cent of the right diaphragmatic hernias are located centrally and usually contain only omentum if the opening is small.

Fig. 2.—Appearance February 10, on bilateral injection of iodized oil with the patient sitting upright. Note upper level of fluid, pneumothorax and collapsed lung.

Reasoning from the changes found at autopsy, this patient had a latent cirrhosis of the liver. The chest and abdominal injury apparently ruptured the dome of the right diaphragm with a resulting omental hernia, which acted as a flap valve. This allowed free access of fluid from the supracolic basin and effectively prevented fluid from accumulating in the abdominal cavity in any demonstrable quantity. The trauma either contributed to or occurred coincidentally with that critical stage of liver dysfunction during which ascites

1. Lewis, Dean: Practice of Surgery, Hagerstown, Md., W. F. Prior Co., Inc. **5**: 18 (chapter 7) 1930.
2. Lewis, Dean: Practice of Surgery **5**: 20 (chapter 7) 1930.

develops. While latent cirrhosis of the liver, often unrecognized during life, occurs commonly, the circumstances present in this case successfully masked a condition which ordinarily would be considered in making the diagnosis. At no period, except for forty-eight hours before death, was there any evidence of demonstrable fluid in the abdominal cavity.

Persistent and rapid reaccumulation of serofibrinous fluid in the pleural cavity occurs most commonly in tuberculosis and malignant disease. Since neither one of these could be demonstrated, the possibility of bronchial fistula was considered particularly in view of the fact that the right lung would not reexpand. An effort to demonstrate the possibility of a bronchial fistula by injection of iodized oil was without result. The roentgenograms show the difference between the compressed bronchial tree of the right lung and the normal bronchial tree of the left lung. I believe that this case illustrates another, although rare, cause of rapid reaccumulation of fluid in the pleural cavity to be considered in differential diagnosis.

Medical Arts Building.

SEVERE DERMATITIS MEDICAMENTOSA FOLLOWING THE ADMINISTRATION OF SULFANILAMIDE

J. OWEN FINNEY, M.D., GADSDEN, ALA.

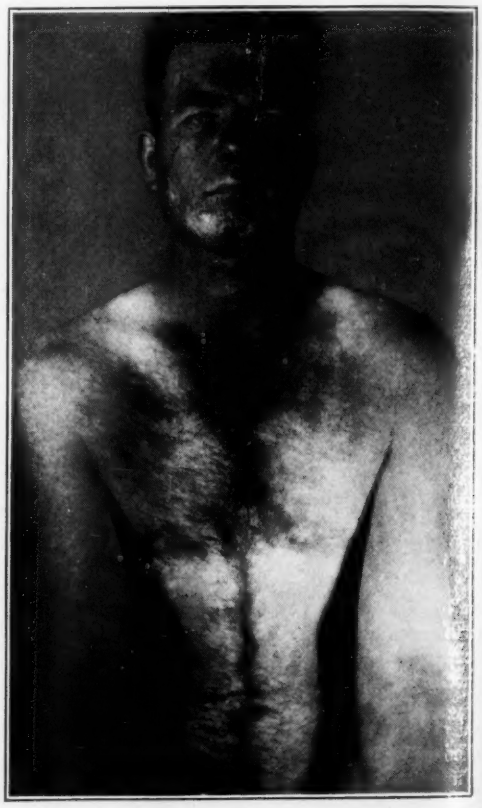
The initial clinical and experimental report of the use of sulfanilamide (para-amino-benzene-sulfonamide) in this country was by Long and Bliss.[1] Subsequent reports have shown its worth in the treatment of hemolytic streptococcus infection,[2] meningococcic infection[3] and gonococcic infection,[4] and one report has been concerned with its apparent efficacy in the treatment of severe gas bacillus infection.[5]

Certain toxic manifestations have been recognized since early in its use. These are dizziness, lassitude, general malaise, cyanosis, sulfhemoglobinemia and fever. Harvey and Janeway[6] reported three cases of acute hemolytic anemia that developed during the administration of the drug, and all three experienced prompt recovery following blood transfusions. Schwentker and his associates[3] mention the fact that a morbilliform rash occasionally occurs in patients when sulfanilamide is used in the treatment of streptococcic infections. Hageman[7] states that such a rash appeared in about one half of his cases that showed a febrile complication following use of the drug. As a rule, all these toxic manifestations have rapidly receded with reduction of the dosage or withdrawal of sulfanilamide.

I have, at the time of this writing, been unable to find a case reported in which the skin manifestations following the use of sulfanilamide have been of sufficient severity to demand hospitalization. For this reason the case reported herein is of importance.

REPORT OF CASE

History.—I. R., a white man, aged 29, married, a farmer, first seen Aug. 7, 1937, complained chiefly of "skin trouble and itching." He had consulted a physician some two weeks previously who told him that he had an acute recurrence of an old gonorrheal prostatitis associated with a cystitis. He had been given a prescription for some tablets, of which he took four four times daily for one day, three four times daily for two days and two four times daily for eight days. (Communication with his physician revealed that the prescription was for sulfanilamide.) About the sixth or seventh day of treatment he began to notice rather marked itching of the skin of the face, arms and chest. He attached no significance to it and continued to take the drug. The symptoms increased in severity and on the last day of treatment he noted the appearance of a rash over his face, arms and chest. During the two days just previous to admission, marked swelling of the face and arms had occurred and the rash had become notable on the back, the buttocks and the dorsum of the feet. He had not been in contact with arsenic to his knowledge and had had no other medication for some time prior to the use of the sulfanilamide. His past history revealed that he had had measles; he had never had any allergic manifestations. The family and personal histories were irrelevant.



Appearance of patient on second day in hospital. There had been some improvement since admission but the lesions were still quite distinct and the edema had not completely subsided.

The patient was obviously very ill and was immediately admitted to the Holy Name of Jesus Hospital for examination and study.

Physical Examination.—The temperature was 101.8 F., the pulse 120, the respiration rate 20 and the blood pressure 130 systolic, 80 diastolic. He was exceptionally well developed and well nourished and was oriented and cooperative though quite uncomfortable. He rubbed various areas of his skin frequently and complained bitterly of generalized itching and of "tightness" of his face. There was a symmetrical maculopapular rash over the body that was most marked on the face, anterior surface of the chest, flexor surface of the arms and extensor surface of the fingers. A similar, though less severe, reaction was present over the buttocks, posterior part of the thighs and the dorsum of the feet. The lesions were in some areas discrete while in others they were confluent, so as to form large patches. There was an associated edema of the face so well marked as to all but close the eyelids; over the chin there was oozing with crusting. Edema of the arms was present to a mild degree. The fingers were so swollen that the patient could not make a "tight fist." The palms and soles were uninvolved. The mucous membranes were of good color and there were no lesions. There was no local or general glandular enlargement. There was no uretheral discharge, and the prostate gland, though mildly boggy, was not tender. The remainder of the examination was not remarkable.

A voided specimen of urine was slightly cloudy with an acid reaction; specific gravity was 1.015, albumin was one

From the Guice-Morgan Clinic.

1. Long, P. H., and Bliss, Eleanor, A.: Para-Amino-Benzene Sulfonamide and Its Derivatives: Preliminary Report, J. A. M. A. **108:** 32-37 (Jan. 2) 1937.
2. Anderson, E. D.: Hemolytic Streptococcus Meningitis, J. A. M. A. **108:** 1591-1592 (May 8) 1937. Mellon, R. R.; Gross, Paul, and Cooper, F. B.: Sulfanilamide and Prontosil in Hemolytic Streptococcus Infections, J. A. M. A. **108:** 1858-1861 (May 29) 1937.
3. Schwentker, F. F.; Gelman, Sidney, and Long, P. H.: The Treatment of Meningococcic Meningitis with Sulfonilamide, J. A. M. A. **108:** 1407-1408 (April 24) 1937.
4. Dees, J. E., and Colston, J. A. C.: Sulfanilamide in Gonococcic Infections, J. A. M. A. **108:** 1855-1858 (May 29) 1937.
5. Bohlman, H. R.: Gas Gangrene Treated with Sulfanilamide, J. A. M. A. **109:** 254-256 (July 24) 1937.
6. Harvey, A. M., and Janeway, C. A.: The Development of Acute Hemolytic Anemia During the Administration of Sulfanilamide, J. A. M. A. **109:** 12-16 (July 3) 1937.
7. Hageman, P. O.: Clinical Experience in the Use of Sulfanilamide at the New Haven Hospital, J. Pediat. **11:** 195-197 (Aug.) 1937.

plus and sugar was not present. The sediment was loaded with white blood cells and there was an occasional large clump. The hemoglobin was 90 per cent (Sahli); the erythrocyte count was 4,900,000; the leukocytes numbered 11,350 with a differential of 65 per cent polymorphonuclear neutrophils, 29 per cent lymphocytes, 4 per cent eosinophils and 2 per cent basophils. The stool was not notable. The nonprotein nitrogen was 31 mg. per hundred cubic centimeters of blood. The fasting blood sugar was 93 mg. per hundred cubic centimeters of blood. The blood Wassermann and Kahn reactions were negative. Stained sediment of the urine showed pus cells but no gram-negative intracellular or extracellular diplococci. A fixed smear of the prostatic fluid showed pus cells but no organisms. The phenolsulfonphthalein renal function test revealed 83 per cent of the dye in two hours. No determination of the sulfanilamide content of the blood was attempted.

Course.—The patient was placed at rest in bed and given a liquid diet. Fluids were forced to 4,000 cc. daily. On admission the lesion so greatly resembled a very early arsenical dermatitis that oatmeal baths were employed at frequent intervals. He obtained such marked symptomatic relief from these baths that they were continued until his discharge from the hospital. No other therapy was given and the symptoms gradually subsided over a period of four days; on the fifth day the patient left the hospital with a normal temperature; the skin was practically clear. Since leaving the hospital he has been seen at frequent intervals and there has been no recurrence of the dermatitis. No attempt has been made to reproduce the condition by giving the patient additional sulfanilamide. The illustration shows the patient on the morning of the second day in the hospital, at which time he had already begun to improve.

SUMMARY

In a case of dermatitis medicamentosa following the administration of sulfanilamide (para-amino-benzene-sulfonamide) the skin manifestations and general condition were of sufficient severity to demand hospitalization of the patient. Recovery was rapid, complete and uneventful with the employment of palliative measures. No attempt was made to reproduce the picture by repeating sulfanilamide after recovery.

American National Bank Building.

EXFOLIATIVE DERMATITIS FOLLOWING SULFANILAMIDE

GORDON B. MYERS, M.D.; E. C. VONDER HEIDE, M.D., AND MATTHEW BALCERSKI, M.D., DETROIT

With full doses of sulfanilamide or related compounds, such toxic manifestations as weakness, lassitude, dizziness, anorexia, nausea, slight cyanosis and mild acidosis occur frequently. According to Long and Bliss,[1] it is not necessary to discontinue the drug when these symptoms appear. With the development of fever or jaundice not attributable to the infection under treatment, withdrawal of the drug is advised. The only grave complications of sulfanilamide therapy reported to date are one case of sulfhemoglobinemia, resulting in death,[2] three fatal cases of agranulocytosis[3] and five cases of acute hemolytic anemia[4] in which recovery occurred after repeated transfusions.

Morbilliform skin eruptions and hyperpyrexia have been described during the course of sulfanilamide therapy,[5] but no severe protracted dermatitis has been reported thus far. The following case of exfoliative dermatitis is therefore presented:

From Receiving Hospital and Wayne University College of Medicine.

1. Long, P. H., and Bliss, Eleanor A.: The Use of Para-Amino-Benzene-Sulfonamide in the Treatment of Infections Due to Beta Hemolytic Streptococci, Pneumococci and Meningococci, South. M. J. **30**: 479 (May) 1937.
2. Frost, L. B. D.: Sulfhemoglobinemia Following Antistreptococcal Therapy, Lancet **1**: 510 (Feb. 27) 1937.
3. Borst, J. G. G.: Death from Agranulocytosis After Treatment with Prontosil Flavum, Lancet **1**: 1519 (June 26) 1937. Young, C. J.: Agranulocytosis and Para-Amino-Benzene-Sulfonamide, Brit. M. J. **2**: 105 (July 17) 1937. Model, A.: Agranulocytosis and Para-Amino-Benzene-Sulfonamide, ibid. **2**: 295 (Aug. 7) 1937.
4. Harvey, A. M., and Janeway, C. A.: The Development of Acute Hemolytic Anemia During the Administration of Sulfanilamide, J. A. M. A. **109**: 12 (July 3) 1937.
5. Unsheim, E.: Zur Behandlung von Kindern mit Prontosil, Arch. f. Kinderh. **110**: 76 (Feb. 12) 1937. Hageman, P. O.: Clinical Experience in the Use of Sulfanilamide at the New Haven Hospital, J. Pediat. **11**: 195 (Aug.) 1937. Hageman, P. O., and Blake, F. G.: A Specific Febrile Reaction to Sulfanilamide, J. A. M. A. **109**: 642 (Aug. 28) 1937.

REPORT OF CASE

A white man, aged 25, contracted gonorrhea in March 1937. After an unsuccessful trial of urethral irrigations and instillations, sulfanilamide therapy was instituted. He received 75 grains (5 Gm.) orally on June 23 and 50 grains (3.3 Gm.) daily thereafter until July 17. The discharge subsided temporarily early in July, only to return after prostatic massage, disappearing again about the middle of July. There were no toxic symptoms whatever until July 17, when he began to notice weakness, lassitude, anorexia, dull aching pain in the epigastrium, giddiness, pain in the eyes, and dryness in the throat and conjunctivae.

Between June 23 and July 17 the patient had been given 1,300 grains (86.6 Gm.) of sulfanilamide. No other medication was administered during this period. The dose of the drug was reduced to 25 grains (1.6 Gm.) July 18, but as the symptoms did not abate it was discontinued July 19. The temperature that day was reported to be 102 F. July 20 the eyelids began to swell and a morbilliform rash appeared on the trunk. The rash soon spread over the entire body and became very

Fig. 1.—Appearance of patient three days after hospitalization, showing distribution of dermatitis on the face and upper extremities.

pruritic, whereas the edema extended to the trunk and extremities. July 25 he noted transient numbness and weakness in the legs. The next day he began to vomit frequently. July 27 he was admitted to the Receiving Hospital and at this time came under our care.

The past history was irrelevant. He had been a labeler in a bottling works. On admission the patient was well developed and well nourished and weighed 175 pounds (79 Kg.). The temperature was 101 F., the pulse 120, the respiration rate 22. There was a bright red, confluent maculopapular eruption over the entire body. In addition, there were many purpuric spots on the hands, feet and legs. No urticarial lesions were present. There was generalized edema, most marked on the face and upper extremities. The lips were distinctly cyanotic. There was no evidence of hemorrhage from the mucous membranes. The heart and lungs were normal. The blood pressure was

118 systolic, 84 diastolic. The liver edge was beneath the costal margin and the spleen was not palpable. No urethral discharge was present. Neurologic examination was negative.

COURSE

The temperature ranged between 100 and 103 F., averaging 101 F. during the first week in the hospital. It reached 98.6 F. August 2 and remained normal after August 4. The pulse was constantly between 110 and 120 during the first week. Nausea and vomiting ceased in three days. The edema was slowly absorbed. The purpuric spots ceased to appear after the first week in the hospital. The skin eruption and pruritus, however, were refractory to aqueous and oily lotions and colloid baths. Desquamation began on the hands and gradually extended over the entire body. At that stage the rash resembled the exfoliative dermatitis due to arsphenamine.

A patch test, August 22, was definitely positive. In addition to an acute dermatitis beneath the patch there was a flare up in the skin eruption elsewhere, with an increase in pruritus, a recurrence of the purpura, and a rise in the eosinophil count from 1,640 per cubic millimeter to 3,760 per cubic millimeter.

The patient was discharged to the outpatient department August 30. A dull red, confluent, papulosquamous eruption was still present on the hands, feet and legs. Prostatic massages produced a thin, purulent discharge which revealed gram-positive staphylococci but no gonococci.

Protocol of Case; Laboratory Examinations

Urinalyses: Specific gravity 1.006 to 1.020, albumin negative, dextrose negative, sediment negative

Blood Cytology:

Date	Hemoglobin	Color Index	Red Blood Cells	White Blood Cells	Neutrophils, Nonfilamented, per Cent	Neutrophils, Filamented, per Cent	Basophils, per Cent	Lymphocytes, per Cent	Eosinophils, per Cent
7/27/37	16.4	0.95	5.45	90,000	47	20	1	7	25
7/28/37	....	....	....	64,500	28	16	..	12	44
7/29/37	18.4	1.10	5.24	75,200	18	21	1	16	44
Transfusion, 200 cc.									
7/30/37	16.6	0.90	5.38	71,200	18	16	..	11	55
7/31/37	15.6	0.90	5.40	45,900	16	18	..	10	55
8/ 2/37	13.2	1.00	4.04	48,600	29	15	..	15	38
8/ 3/37	13.4	0.90	4.34	26,800	33	4	..	20	43
8/ 4/37	13.0	0.80	4.64	39,100	15	15	..	25	45
8/ 5/37	12.8	1.00	4.08	33,400	10	8	1	27	54
8/ 7/37	12.4	0.90	4.31	22,000	16	9	..	32	43
8/11/37	13.8	1.00	4.38	19,452	18	20	..	24	38
8/19/37	12.2	0.80	4.50	13,700	16	24	..	12	47
8/24/37	14.4	0.90	4.65	13,450	30	18	..	28	23

Bleeding and Clotting Time:

7/27/37 Bleeding time 5 min. 30 sec; clotting time 3 min. 15 sec.; platelets, 201,650
7/30/37 Rumpel-Leede test markedly positive
8/ 4/37 Bleeding time 2 min. 30 sec.; clotting time 4 min.
8/26/37 Bleeding time 4 min. 30 sec.; clotting time 5 min.

Spectroscopic Examination: No evidence of methemoglobin or sulfhemoglobin

Serologic Reaction: Negative

Blood Chemistry and Renal Function Tests:

7/28/37 Urea 19.2; chlorides 363.0; carbon dioxide combining power = 55.0 vol. %
7/30/37 Serum albumin 3.03%
Serum globulin 1.08%; carbon dioxide combining power = 47.0 vol. %
8/ 9/37 Carbon dioxide combining power = 28.0 vol. %
8/18/37 Urea clearance (maximal), 72 cc. cleared per minute; carbon dioxide combining power = 61.0 vol. %

Serum Pigmentation:

7/28/37 Icterus index 21.0; van den Bergh, moderate immediate direct reaction; bilirubin 2.0 mg. %
7/30/37 Icterus index 15.0; van den Bergh, weak immediate direct reaction; bilirubin 1.02 mg. %
8/ 9/37 Icterus index 7.0
8/17/37 Icterus index 7.5

Liver Function Tests:

	Urobilinogen (Highest Positive Dilution Detectable in Urine)
7/28/37	1:60
7/29/37	1:90
7/30/37	1:50
8/ 2/37	Trace
2/ 5/37 and onward.....	Trace

Hippuric Acid Test:

7/30/37 2:58 Gm. benzoic acid recovered as hippuric acid in 2 hours

Oral Galactose Tolerance Test (40 Gm.):

8/ 5/37 1.70 Gm. galactose recovered

COMMENT

The fact that sulfanilamide was the only drug taken before the eruption appeared, together with the positive patch test, would indicate that it was responsible for the dermatitis. Since the blood urea level and the urea clearance test were normal in this case, the poisoning cannot be attributed to renal insufficiency. It is noteworthy that 50 grains (3.3 Gm.) was taken daily for twenty-five days before any toxic symptoms developed. Such symptoms as weakness, lassitude, dizziness and anorexia, which have been considered of minor importance, preceded the serious toxic manifestations by three days, during which only an additional 25 grains (1.6 Gm.) of the drug was taken. The wisdom of administering sulfanilamide in such doses over so long a period without sulfanilamide determinations of the blood may be seriously questioned.

Certain other features of this case deserve brief comment. The leukocytosis and eosinophilia were much greater than in the cases of arsenical exfoliative dermatitis studied by Towle and Swartz,[6] in which the total leukocyte count averaged 12,400 and the eosinophils 10 per cent. The blood picture was not that of a leukemia. The purpura was probably due chiefly to increased capillary permeability. The jaundice was short in duration and was associated with slight transient impairment of hepatic function. Although there was distinct cyanosis, no evidence of sulfhemoglobin or methemoglobin was found on spectroscopic examination. The carbon dioxide combining power of the blood fell from 55 volumes per cent on July 28 to 28 volumes per cent on August 9. During this period the patient received 45 grains (3 Gm.) of calcium carbonate and 45 grains of calcium lactate daily in addition to a high carbohydrate diet and intravenous administration of dextrose. The acidosis quickly cleared up after the administration of sodium bicarbonate, which had previously been avoided because of the edema.

Fig. 2.—Distribution of purpura on foot three days after hospitalization.

SUMMARY

A severe exfoliative dermatitis accompanied by edema, purpura, fever, marked leukocytosis and eosinophilia, moderate acidosis and transient jaundice developed in a patient who had taken 1,325 grains (88.3 Gm.) of sulfanilamide over a period of twenty-eight days for the treatment of gonorrheal prostatitis.

6. Towle, H. P., and Swartz, J. H.: A Study of the Blood in Some Common Diseases of the Skin, Arch. Dermat. & Syph. **9**: 554 (May) 1924.

Special Article

DEATHS DUE TO ELIXIR OF SULFANILAMIDE-MASSENGILL

REPORT OF SECRETARY OF AGRICULTURE SUBMITTED IN RESPONSE TO HOUSE RESOLUTION 352 OF NOV. 18, 1937, AND SENATE RESOLUTION 194 OF NOV. 16, 1937

During September and October of 1937 at least seventy-three persons died as a direct result of taking the drug known as "Elixir Sulfanilamide." Twenty other persons who took the "elixir" died, but it has not yet been established that this drug was exclusively responsible. The ninety-three deaths occurred in fifteen states, as far east as Virginia, as far west as California.

"Elixir Sulfanilamide" was manufactured and sold by the S. E. Massengill Company of Bristol, Tenn. According to the firm's books, 240 gallons was manufactured. The entire amount has been accounted for.

Before the "elixir" was put on the market, it was tested for flavor but not for its effect on human life. The existing Food and Drugs Act does not require that new drugs be tested before they are placed on sale. . . .

Since the Federal Food and Drugs Act contains no provisions against dangerous drugs, seizures had to be based on a charge that the word "elixir" implies an alcoholic solution, whereas this product was a diethylene glycol solution. Had the product been called a "solution" rather than an "elixir," no charge of violating the law could have been brought.

Of the 240 gallons manufactured, 228 gallons and 2 pints has been seized under federal and state laws, destroyed, collected as laboratory samples, or wasted by spillage and breakage. Eleven gallons and 6 pints was dispensed on prescriptions or over the counter sales. Of this amount, about half was consumed and caused the deaths; the other half was retrieved before consumption.

The lethal effect of the "elixir" was due to its content of diethylene glycol. . . .

Sulfanilamide is the name of one of a group of closely related chemicals first reported in European medical literature of 1935 to have been used for drug purposes. . . . An editorial from THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, attached as exhibit A,[1] shows that sulfanilamide is potentially dangerous but that properly used it may be brilliantly successful in treating various infections.

The fatal "elixir" was rushed onto the market without adequate test to determine whether or not diethylene glycol may be safely used as a solvent for sulfanilamide, despite previously published reports in scientific literature showing that diethylene glycol might be dangerous when taken internally. A few simple and inexpensive tests on experimental animals would have quickly demonstrated the toxic properties of both diethylene glycol and the "elixir."

It will be observed that the preparation is a semisecret one, that the presence of diethylene glycol is not disclosed, and that no warning of danger appears.

Most of the drug was administered on physicians' prescriptions.

HOW THE "ELIXIR" WAS PRODUCED

Dr. Samuel Evans Massengill is sole owner of the S. E. Massengill Company, of Bristol, Tenn. He holds the degree of Doctor of Medicine and was licensed to practice medicine in 1900. His letterhead bears the statement "Purveyor to the Professions of Medicine and Pharmacy since 1897."

Mr. Harold Cole Watkins, chief chemist and pharmacist of the company, holds a degree of Pharmaceutical Chemist. Since 1900 he has been engaged as pharmaceutical, analytical and research chemist by various firms. He joined the Massengill Company in 1935.

For some time before putting "Elixir Sulfanilamide" on the market, the S. E. Massengill Company had been marketing sulfanilamide in capsule and tablet form. In June 1937 the firm's salesmen reported a demand for the drug in liquid form. Near the end of July Mr. Watkins, according to his own statement, undertook the problem of finding a suitable liquid vehicle for sulfanilamide. Since sulfanilamide is insoluble in the various liquids commonly employed in making medicines, he tried a number of other solvents. Diethylene glycol was found to dissolve as much as 75 grains of sulfanilamide per fluidounce, but in that concentration it tended to separate out on chilling. Accordingly he decided on 40 grains per fluidounce as a stable preparation and devised the following working formula:[2]

Sulfanilamide	58½	pounds
Elixir flavor	1	gallon
Raspberry extract	1	pint
Saccharin soluble	1	pound
Amaranth solution ⅛	1½	pints
Caramel	2	fluidounces
Diethylene glycol	60	gallons
Water, q. s.	80	gallons

According to Mr. Watkins, no tests were made to determine the toxicity of either the separate ingredients or the finished product, or to determine by well known methods available for the purpose whether or not the sulfanilamide decomposed in the diethylene glycol. The so-called control laboratory merely checked the "elixir" for appearance, flavor and fragrance. Dr. Massengill confirmed Mr. Watkins' statement that no experimental animals were used or clinical tests of any kind made to determine either the effectiveness or the toxicity of the drug before it was put on the market. . . .

Distribution of both commercial [633 shipments] and sample [671-one and two ounce bottles] lots extended over the period from Sept. 4, 1937, up to and including Oct. 15, 1937.

THE FOOD AND DRUG ADMINISTRATION STEPS IN

The first word of deaths from an unidentified sulfanilamide preparation reached the Food and Drug Administration on Oct 14, 1937, through a telephone call from a New York physician associated with a large drug manufacturing concern. He repeated advices, presumably received through professional or trade contacts, that fatalities had occurred at Tulsa, Okla.[3]

This report was released to the press on November 26 and is reproduced with minor deletions.—ED.

1. Sulfanilamide—A Warning, editorial, J. A. M. A. **109**: 1128 (Oct. 2) 1937.—ED.

2. This formula is in substantial agreement with that determined by analysis by Schoeffel et al. of the A. M. A. Chemical Laboratory, J. A. M. A. **109**: 1531 (Nov. 6) 1937.—ED.

3. The headquarters office of the A. M. A. also telegraphed to the Food and Drug Administration on the same day concerning the presence in the mixture of diethylene glycol.—ED.

Immediately instructions to investigate the report were issued by telegraph to the Kansas City Station of the Food and Drug Administration, which is the nearest station to Tulsa. A representative of the administration arrived in Tulsa the following day. He reported by telegraph on Saturday, October 16, that nine deaths had already occurred in Tulsa, including eight children with streptococcic sore throat and one adult with gonorrhea, and that all had taken a product labeled "Elixir Sulfanilamide, The S E. Massengill Company, Manufacturing Pharmacists, Bristol, Tenn.-Va." [Seizure of all outstanding shipments was immediately ordered.]

Shipping records showed that the suspected "elixir" had come from a Massengill establishment in Kansas City, to which the station immediately sent inspectors. Also an inspector from the Cincinnati station, which is the nearest station to Bristol, and a medical officer from the administration's headquarters at Washington, were sent at once to Bristol.

Inspectors from the New York and San Francisco stations were assigned to investigate distributions from these points.

It was learned that the Massengill Company, following reports of the poisonous effects of the "elixir," had sent out approximately 375 telegrams from Bristol and additional telegrams from its branch houses totaling, according to the firm's statement, some 1,100 in all, requesting the return of outstanding shipments. The texts of these wires follow:

From the Bristol office to customers, on October 15:

"Do not use elixir sulfanilamide shipped. Return our expense."

To salesmen on the same date:

"Elixir sulfanilamide discontinued. Pick up as rapidly as possible all sold in your territory."

From the Kansas City branch to jobbers, druggists and doctors who had received the product, on October 15:

"Have withdrawn product elixir sulfanilamide. Please return unusued stocks immediately."

From the New York branch to customers on October 16:

"Return for credit all elixir sulfanilamide you have of our manufacture Stop. We shall appreciate prompt attention."

On or about October 15, on telegraphed instructions from the Bristol office, the San Francisco branch of the firm instructed its salesmen to have outstanding stocks returned. However, investigation revealed that no attempt had been made by that branch to communicate directly with dealers and doctors.

On October 16 the Bristol office wired the New York branch:

"Discontinue sale elixir sulfanilamide Stop. Wire all salesmen immediately pick up sold Stop. Wire direct all customers sold to return stock unusued."

On the same date the New York branch wired to thirteen of its salesmen who were thought to have sold the "elixir" and wrote to its remaining twenty-six salesmen, one of whom was in Puerto Rico. Telegrams and letters were practically identical:

"Discontinue the sale of elixir of sulfanilamide. Pick up and return all orders of this item previously sold. We are discontinuing immediately the manufacture of this item."

Since these telegrams and letters gave no indication of the dangerous character of the product and were not calculated to impress receivers with the emergency character of the call for returning the goods, the inspector assigned to the Bristol office insisted that the firm issue the following telegram, dated October 19, to all persons who were listed as having received shipments of the "elixir" from Bristol:

"Imperative you take up immediately all elixir sulfanilamide you dispensed. Product may be dangerous to life. Return our expense."

Following similar insistence by the San Francisco, Kansas City and New York inspectors, the branches at those points sent . . . similar telegrams to all consignees, on or about October 19.

As a result of these telegrams, large quantities of the "elixir" were returned to the manufacturer's establishments and there taken under local or federal control. But the extremely dangerous character of the drug necessitated the most searching check to guarantee, as far as humanly possible, its complete apprehension. Practically the entire field force of 239 Food and Drug Administration inspectors and chemists were assigned to the work. They had the wholehearted and effective cooperation of state and local food, drug and health authorities. As an additional aid, warnings by newspaper and radio were broadcast.

In spite of the manufacturer's telegrams, many shipments were found still in dealers' hands. Innumerable prescriptions filled from these lots, as well as from shipments returned to the manufacturer, were found to have been only partly consumed by the patient and so were recovered.

The essential steps in tracing and apprehending the poisonous drug were (*a*) listing names and addresses of consignees, dates of shipment, and amounts shipped from the four establishments of the manufacturer; (*b*) following these to the primary consignees and seizing, if still intact in their possession; (*c*) if partially used, seizing the residue and following and procuring the distributed portions if not already consumed; (*d*) checking on lots reported returned to the manufacturer and definitely ascertaining whether such returned lots were intact; (*e*) if returned lots were not intact, searching for dispensed portions. . . .

The magnitude of the task of listing distributions is indicated by the fact that thousands of order slips had to be examined, one by one, in the four distributing houses and that in some cases this procedure had to be repeated in wholesale and retail drug stores to determine what redistributions had occurred. In one establishment alone, 20,000 sales slips were examined.

The task was complicated by the fact that distribution was not made exclusively on physicians' prescriptions, which normally would have recorded the name of the patient, but that over the counter sales were made to lay purchasers, who in some cases were entirely unknown to the druggist. In some instances, doctors had no record of the names and addresses of patients for whom they had prescribed, or the names recorded were fictitious.

The task of interviewing promptly the approximately 200 salesmen employed by the Massengill Company, in order to account for salesmen's samples and to check the distribution of physicians' samples and commercial shipments, presented serious difficulties in some cases. A typical instance was that of a salesman whose territory includes part of Maryland and Virginia. He was first reported to be at a hotel in Washington, D. C. He was not there. Forwarding addresses at Jackson,

Mich., and in Baltimore were investigated only to learn that these were for another man of the same name. After four days' search, the salesman was found at University Park, Md. One salesman in Texas was thoroughly uncooperative and was put in jail by the state authorities before he decided to reveal the necessary information.

At East St. Louis, Ill., forty-nine prescriptions, all for colored people, were filled from two shipments. The only identification on some of the prescriptions were such notations as "Betty Jane, 9 months old" or "Mrs Jackson (no address)." In a very few instances, recipients of prescriptions bearing no identification have not yet been found, although every effort has been made to warn them by newspaper and radio.

THE PROBLEM BEFORE PHYSICIANS AND PHARMACISTS

Most of the physicians and pharmacists involved in dispensing the "elixir" cooperated willingly and effectively in apprehending outstanding prescriptions. . . .

In contrast was the attitude of a South Carolina doctor, who told the inspector he had dispensed 1 pint 15 fluidounces to three white patients and two Negroes, whose names he did not reveal. He insisted that none of these patients had died. Information acquired by the inspector from other sources showed that the doctor had administered the elixir to seven patients, that three survived, and that a white man, a white girl, and two Negro men had died. One of the fatal prescriptions was traced through neighborhood gossip describing the symptoms of the fatal illness of a Negro employee of a lumber mill. The inspector recognized the symptoms as characteristic of "elixir" poisoning and through the mill superintendent found the victim's sister. She remembered that the doctor had given her brother some red medicine about October 2 or 3. She said that, in accordance with their custom, all medicines, glasses, spoons, etc., had been placed on the grave, which was about 1½ miles back in the fields. Accompanied by the Negroes, the inspector walked to the wooded knoll with its single mound of fresh earth on which lay several bottles, dishes and spoons. One 4 ounce bottle contained about one ounce of the "elixir." It bore the weatherbeaten but legible prescription label of the doctor.

An inspector investigating a Georgia drug store listed as having received one gallon of the "elixir" was informed that the shipment had been returned to the manufacturer at Bristol after only one lot of 6 ounces had been dispensed for one patient. Subsequent investigation showed that this patient had suffered no ill effects. But the inspector assigned at Bristol for the purpose of checking returned lots found 12 instead of 6 ounces missing from the gallon bottle returned by this druggist. Further investigation showed that two additional lots had been dispensed and had caused two deaths.

EFFECTS OF THE DRUG

The victims of the "elixir" were ill from about seven to twenty-one days. They suffered intense pain. All exhibited very much the same symptoms: stoppage of urine, severe abdominal pain, nausea and vomiting, and stupor; convulsions preceded death in some cases. Many persons who took the drug discontinued its use with the onset of unfavorable symptoms and recovered. One person took as much as 7½ fluidounces without ill effect. One child died from less than 2 fluidounces.

ACTION UNDER THE LAW

Twenty-five seizures of the "elixir" were effected under the federal Food and Drugs Act. Many lots were seized or embargoed by local officials through action under state or city laws.

The distribution of the shipments from the four establishments maintained by the manufacturer of the "elixir" and the deaths that occurred are shown in the map attached as exhibit B.[4]

Citations are already in preparation for issuance to the manufacturer, in accordance with established procedure, calling on him to show cause why the cases should not be referred to the federal courts for criminal prosecution.

In September 1934 and March 1937 the S. E. Massengill Company was convicted in criminal prosecutions and paid fines for violations of the Food and Drugs Act, as recorded in notices of judgment attached as exhibit C. Also included in this exhibit is a notice of seizure of a shipment of one of this firm's drugs.

Records of the Post Office Department show that in 1929 H. C. Watkins, the Massengill Company chemist who made the "elixir," was distributing a medicine represented to reduce weight, to bring about "perfect slenderness" and to cause the body to acquire "a trim, youthful, athletic look." On Oct. 30, 1929, the Watkins Laboratories and others were cited by the Solicitor of the Post Office Department to show cause why a fraud order should not be issued. Mr. H. C. Watkins filed a stipulation with the department, agreeing that the sale of the product would be abandoned and not resumed at any future time.

LIMITATIONS OF THE LAW

As indicated earlier in this report, the only basis of action under the Food and Drugs Act against the interstate distribution of the "elixir" was the allegation that the word implies an alcoholic solution whereas the product was a diethylene glycol solution. The fact that the law contains no specific definition of "elixir" may be responsible for Dr. Massengill's statement in his letter to the American Medical Association, carried in the press of November 3: "I have violated no law."

Most drug manufacturers recognize a responsibility to the public far greater than that imposed by existing law. Some are known to have considered making a solution of sulfanilamide in diethylene glycol before the "elixir" was put on the market but abandoned the idea on investigating the toxicity of the solvent. But the attitude of some drug makers is exemplified in Dr. Massengill's statement carried by the press on October 23:

"My chemists and I deeply regret the fatal results but there was no error in the manufacture of the product. We have been supplying legitimate professional demand and not once could have foreseen the unlooked-for results. I do not feel that there was any responsibility on our part. The chemical sulfanilamide had been approved for use and had been used in large quantities in other forms, and now its many bad effects are developing."

That evidence of possible danger from the internal administration of diethylene glycol was available prior to the marketing of the "elixir" is shown by the attached exhibit D.[5]

That a few simple tests on experimental animals would have demonstrated the lethal properties of the elixir is evident from the work reported by the American Medical Association in exhibit E.[6] These results were confirmed independently by the Division of Pharmacology of the Food and Drug Administration in work yet unpublished.

4. A map showing the number and distribution of the deaths was published in THE JOURNAL, November 20, p. 1724.—ED.

5. von Oettingen, W. F., and Jirouch, E. A.: The Pharmacology of Ethylene Glycol and Some of Its Derivatives in Relation to Their Chemical Constitution and Physical Chemical Properties, J. Pharmacol. & Exper. Therap. **42**: 355 (Aug.) 1931.—ED.

6. Elixir of Sulfanilamide-Massengill: Chemical, Pharmacologic, Pathologic and Necropsy Reports; Preliminary Toxicity Reports on Diethylene Glycol and Sulfanilamide, special article from the A. M. A. Chemical Laboratory, J. A. M. A. **109**: 1531 (Nov. 6) 1937.—ED.

While the "elixir" incident has been spectacular and has received much publicity, aside from the brevity of the period in which the killings occurred it is but a repetition of what has frequently happened in the past in the marketing of such dangerous drugs as dinitrophenol, cinchophen and other toxic substances.

It is worthy of note that, shocking as these instances have been, the actual toll in deaths and permanent injury from potent drugs is probably far less than that resulting from harmless nostrums offered for serious disease conditions. In these cases the harmful effect is an indirect one. Sick people rely on false curative claims made for worthless concoctions and thus permit their disease to progress unchecked. It may be too late when they lose confidence in the nostrum and seek rational treatment.

RECOMMENDATIONS FOR LEGISLATION

To protect the public from drugs which, like the "elixir," are dangerous because of their inherent toxicity, it is the department's recommendation that legislation be enacted to provide at least the following:

1. License control of new drugs to insure that they will not be generally distributed until experimental and clinical tests have shown them to be safe for use. The definition of what constitutes a new drug should include (*a*) substances which have not been used sufficiently as drugs to become generally recognized as safe, (*b*) combinations of well known drug substances where such combinations have not become generally recognized as safe, and (*c*) well known drug substances and drug combinations bearing label directions for higher dosage or more frequent dosage or for longer duration of use than has become generally recognized as safe.

Exemption should be made for new drugs distributed to competent investigators for experimental work. A board of experts should be provided who will advise the Secretary of Agriculture on the safety of new drugs.

It is the department's view that no other form of control will effectively safeguard the public from the dangers of premature distribution of new drugs. To increase the penalties for violations and to require label disclosure of ingredients would be helpful but by no means fully adequate.

In the interest of safety, society has required that physicians be licensed to practice the healing art. Pharmacists are licensed to compound and dispense drugs. Electricians, plumbers and steam engineers pursue their respective trades under license. But there is no such control to prevent incompetent drug manufacturers from marketing any kind of lethal potion. It should be remembered that Dr. Massengill and his chemist Watkins are far better equipped from the standpoint of technical training than many other persons now engaged in the manufacture of drugs.

2. Prohibition of drugs which are dangerous to health when administered in accordance with the manufacturer's directions for use. This would provide a more appropriate basis of action than that on which proceedings were instituted against the "elixir." A number of dangerous drugs are now on the market against which not even a trivial charge of violation can be made.

3. Requirement that drug labels bear appropriate directions for use and warnings against probable misuse. Much injury results from insufficient directions and from lack of warning against overdosage, or administration to children, or use in disease conditions where the drug is dangerous, or possibility of drug addiction.

4. Prohibition of secret remedies by requiring that labels disclose fully the composition of drugs. Many foreign countries now impose this requirement. Many drugs manufactured in the United States are exported to such countries under labels bearing such disclosure. The same drugs are sold to our citizens under labels that give no hint of their composition.

The physician, and the consumer who acts as physician to himself, both have a right to know what they administer.

Many poisoning cases result from choice of the wrong bottle from the home medicine cabinet, or from bottles left within the reach of small children. In such cases attending physicians are able to proceed intelligently and administer the proper antidotes or other treatment only if labels carry full disclosure of composition. Delays in obtaining this information by communicating with the manufacturer may often mean the difference between life and death.

Physicians are also handicapped in arriving at a correct diagnosis and beginning appropriate treatment when patients come to them after unsuccessful attempts at self medication with secret remedies. The effect of such remedies may give rise to symptoms leading to erroneous diagnosis. But even if the diagnosis is correct, the kind of treatment to be used may depend on what the patient has been taking. Again, in such circumstances, label declaration of composition may mean the difference between life and death.

The foregoing recommendations are limited to provisions which the department believes should be enacted to safeguard the public from the dangers of drugs of one type. That type includes the inherently toxic drugs, such as the "elixir," dinitrophenol and cinchophen. Many additional points should be considered if adequate protection is to be extended against even more widespread dangers to health and other abuses of public welfare arising from the inadequate control authorized by the present law over various other types of drugs.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. HOWARD A. CARTER, Secretary.

GENERAL ELECTRIC MODEL F QUARTZ-MERCURY ULTRAVIOLET LAMP ACCEPTABLE

Manufacturer: General Electric X-Ray Corporation, 2012 Jackson Boulevard, Chicago.

This Model F Quartz-Mercury Ultraviolet Lamp is designed for use in the office or hospital under the direction of a physician. It is arranged to operate solely on alternating current, but special equipment may be procured where only direct current is available. The source is a quartz-mercury Uviarc burner, similar to the previously accepted source (THE JOURNAL, Dec. 16, 1933, p. 1967) but designed so as to minimize obstruction to direct or reflected radiation. It builds up in four minutes and cools in approximately six minutes. The unit is self starting without tilting.

General Electric Model F Quartz-Mercury Ultraviolet Lamp.

The reflector is chromium plated with a mat finish. The burner housing is equipped with easily manipulated shutters, which provide a means of closing off the radiation without turning off the burner. A self-winding tape measure for reading the distance directly from the burner to the skin of the patient is built into the burner housing. The burner housing can be adjusted to treat a patient prone, sitting or even standing. The transformer is mounted in an ornamental base. It weights the lamp, thus preventing it from tipping easily. The 50 or 60 cycle lamps weigh 85 pounds; the 25 cycle one weighs approximately 100 pounds. The on-and-off switch, the only control provided, is operated by a foot switch projecting from the base.

The quartz-mercury vapor burner consists of a single quartz tube approximately three-fourths inch in diameter and 6 inches long, to each end of which is sealed an electrode similar in appearance to the anode of a standard Uviarc. Its over-all length is about 10¼ inches. The burner operates directly from alternating current through a special transformer located in the base of the lamp. No tubes, tungars, rheostats, voltmeters or other devices or adjustments are required. The transformer is provided with taps to compensate for various line voltages, which are adjusted at the time of installation and need not be touched afterward unless the line voltage should change con-

siderably. As the line demand is low, approximately 400 watts, the lamp may be operated from practically any convenient outlet of suitable voltage and frequency.

At the 30 inch treatment distance the extreme limits of the radiation field measure approximately 46 by 54 inches. At a 40 inch treatment distance it measures approximately 61 by 108 inches. The intensity and quality of the radiation are similar to those produced by the Council-accepted models A, B and C. The time required for an erythema dose is about one minute at a distance of 30 inches.

The burner housing is mounted on a bracket atop the upper part of a two section telescopic tube column counterbalanced by means of a spring within the column. The housing, if permitted, will assume a position approximately half way between the lowest and highest position. The range of adjustment is between 7 feet and 4 feet, 10 inches from the floor.

Lamps are available for operation at 115 or 230 volts, 25, 50 or 60 cycles. The actual frequency available must be within two cycles of the rated frequency.

The lamp was placed in a clinic acceptable to the Council for investigation. Tests were made to substantiate the erythemic claims made for it by the manufacturer. It was found to produce a minimal erythema in one-half minute or less at 30 inches distance, in the average person. It appears to be a satisfactory device for the administration of ultraviolet radiation.

In view of the foregoing report, the Council on Physical Therapy voted to include the General Electric Model F Quartz-Mercury ultraviolet lamp in its list of accepted devices.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

THE STATUS OF MANDELIC ACID

A report on mandelic acid by Dr. William F. Braasch, Rochester, Minn., was endorsed by the Council and published as a preliminary report (THE JOURNAL, March 27, 1937, p. 1033). The conclusion to this report was as follows:

> It would appear that the oral administration of mandelic acid is followed by elimination of bacillary infection in the urinary tract in a large percentage of uncomplicated cases. There is no clinical evidence to indicate that it is a severe renal irritant in the presence of a normal renal function, provided it is not continued longer than two weeks. Its use is contraindicated when there is evidence of renal insufficiency because of the possibility of causing renal irritation and since [in this condition] it is usually not excreted in sufficient concentration to be bactericidal.

Dr. Braasch's report stressed the undesirable effects of mandelic acid therapy. These included occasional nausea, diarrhea, renal irritation and hematuria. Since the appearance of the preliminary report, other cases presenting these symptoms have been recorded, although evidence of serious or permanent renal damage has not been presented.

The toxic symptoms do not seem to be of sufficient intensity or duration to contraindicate the cautious use of the drug. The possibility of their occurrence must, however, be emphasized and is sufficient reason for insisting that the drug be used only under the careful supervision of the physician.

Owing to the somewhat enthusiastic reports which have appeared in the literature, mandelic acid is already extensively employed. In Braasch's report it was shown that the drug is bactericidal in a large percentage of cases of uncomplicated urinary infection, being especially effective in bacillary infections. It is helpful as a preliminary to instrumentation or surgical treatment of the urinary tract. In some cases in which the bacteria are not completely eliminated from the urine, there has been repeated reduction in the degree of infection and improvement in subjective symptoms. Further experience has not invalidated the general truth of these claims.

The Council voted, therefore, to accept mandelic acid for inclusion in New and Nonofficial Remedies.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

MANDELIC ACID.—Phenyl-glycollic acid, alpha-hydroxy alpha-toluic acid; the synthetically prepared racemic (*d-l*) compound of the formula $C_6H_5CH(OH)COOH$.

Actions and Uses.—Mandelic acid is a nonmetabolizable substance which when administered by mouth is excreted unchanged in the urine, and if the p_H of the urine is kept at 5.5 or less it is rendered bactericidal or bacteriostatic against Escherichia coli, Aerobacter aerogenes, Streptococcus faecalis and organisms of the Proteus, Pseudomonas, Alcaligenes, Salmonella and Shigella groups. The acidity should be controlled by frequent determinations of the p_H. In cases in which the acidity is not reduced to p_H 5.5 or less, other acidifying agents such as ammonium chloride, ammonium nitrate or nitrohydrochloric acid may be administered concurrently providing there are no contraindications; the ketogenic diet may also be employed. Fluid intake should be restricted to an amount not exceeding 1,200 cc. daily. It is usually neither necessary nor advisable to continue mandelic acid therapy longer than from twelve to fourteen days, as renal irritation may ensue. Nausea, diarrhea, dysuria and hematuria may also occur occasionally, requiring reduction in dosage or interruption of therapy. Mandelic acid should not be administered in the presence of renal insufficiency, as an inadequate concentration is obtained in the urine; renal irritation may result, and serious acidosis may occur from retention of the acid.

Dosage.—The usual dosage is 3 Gm. four times a day either as the free acid or in the form of the sodium or ammonium salt. An additional acidifying agent is usually required when the sodium salt is employed.

Mandelic acid is prepared by allowing sodium cyanide to react with the sodium bisulfite addition compound of benzaldehyde. The mandelonitrile thus formed is isolated and hydrolyzed to give the impure acid, which is separted and purified.

Mandelic acid is a white, crystalline compound which gives a colorless, clear solution in water, alcohol and alkali. It is odorless and possesses a sharp, salty taste. The solubility is 16 Gm. in 100 cc. water at 20 C.; 53.6 Gm. dissolve in 100 cc. ethyl alcohol at 16.5 C. The melting point of the substance is 118-120 C. (microscopic heating stage).

Mandelic acid is slightly unstable, slowly turning yellow when exposed to light; reacts with alkalis and basic substances. A saturated aqueous solution reacts strongly acid to congo red test paper and slightly acid to cresol red paper.

Dissolve about 0.25 Gm. of mandelic acid in 10 cc. of water and add two drops of ferric chloride test solution: a bright yellow color is produced.

Dissolve about 0.25 Gm. of mandelic acid in 5 cc. of water in a test tube; to this solution add 5 cc. of concentrated sulfuric acid, agitate the test tube and contents for a few seconds; then add 10 cc. of concentrated sulfuric acid, and mix contents by a twirling motion: a purple color slowly forms if the test tube is allowed to stand for a few minutes, and a strong odor of benzaldehyde is noticed.

The moisture content of mandelic acid should not exceed 0.5 per cent. *d-l* mandelic acid complies with the U. S. P. tests for heavy metals. The U. S. P. XI (page 471) chloride test for 1 Gm. should not exceed the turbidity produced by 0.05 cc. of 0.02 normal hydrochloric acid in 50 cc. of solution.

The ash from 0.1 Gm. *d-l* mandelic acid is negligible.

Transfer about 0.1 Gm. *d-l* mandelic acid, accurately weighed to a beaker, add 25 cc. of CO_2 free, distilled water and titrate with 0.1 normal sodium hydroxide using phenolphthalein as an indicator: the alkali used is equivalent to not less than 99.3 per cent nor more than 100 per cent mandelic acid (each cubic centimeter of 0.1 normal sodium hydroxide is equivalent to 0.0152 Gm. mandelic acid).

Mandelic Acid-Mallinckrodt.—A brand of mandelic acid-N. N. R.

Manufactured by Mallinckrodt Chemical Works, St. Louis. No U. S. patent or trademark.

BISMUTH SUBSALICYLATE (See New and Nonofficial Remedies, 1937, p. 133).

Ampoules Bismuth Subsalicylate 2 grains (0.13 Gm.) in Oil, 1 cc.: A suspension of bismuth subsalicylate-U. S. P. 0.13 Gm., Chlorbutanol (chloroform derivative) 0.03 Gm., and distilled water 0.10 cc., in sufficient olive oil to make 1 cc.

Prepared by Sharp & Dohme, Philadelphia and Baltimore. No U. S. patent or trademark.

Bismuth Subsalicylate in Oil, 2 ounce bottle: Each cubic centimeter contains a suspension of bismuth subsalicylate-U. S. P. 0.13 Gm., Chlorbutanol (chloroform derivative) 0.03 Gm., and distilled water 0.10 cc., in sufficient olive oil to make 1 cc.

Prepared by Sharp & Dohme, Philadelphia and Baltimore. No U. S. patent or trademark.

SULFANILAMIDE-SQUIBB (See THE JOURNAL, July 31, 1937, p. 358, Oct. 30, 1937, p. 1456; and Supplement to New and Nonofficial Remedies, 1937, p. 19).

The following dosage form has been accepted:

Sulfanilamide Tablets, 7½ grains.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, DECEMBER 11, 1937

THE COUNCIL ON INDUSTRIAL HEALTH

For more than two years the Board of Trustees of the American Medical Association had under consideration the advisability of establishing a council the function of which would be to deal with matters pertaining to occupational diseases and other phases of the subject of industrial health.

A committee of the Section on Dermatology and Syphilology has for several years interested itself in the problems growing out of the widespread incidence of industrial dermatoses, and at the Kansas City session in 1936 a resolution was submitted to the House of Delegates by Dr. A. R. McComas of Missouri, requesting the Board of Trustees to continue and enlarge its study of industrial hygiene and occupational diseases and to provide for active participation in well directed efforts designed to effect better control of occupational disease.

In March 1937 a conference was held in Chicago, which was participated in by the members of the Executive Committee of the Board of Trustees and by a group of distinguished physicians who have given special study to the general subject of industrial hygiene. At the Atlantic City session the Board of Trustees submitted to the House of Delegates the recommendation of this conference, to the effect that a council, to be known as the Council on Industrial Health, be established and maintained by the American Medical Association. This recommendation received the approval of the House of Delegates, and the Board of Trustees has taken steps to establish the Council on Industrial Health and has appointed the following members, all of whom have agreed to serve: Drs. Stanley J. Seeger, Milwaukee, chairman; Harvey Bartle, Philadelphia; Warren F. Draper, Washington, D. C.; Leroy U. Gardner, Saranac Lake, N. Y.; Morton R. Gibbons, San Francisco; H. H. Kessler, Newark, N. J.; A. D. Lazenby, Baltimore; Earl D. Osborne, Buffalo, and C. W. Roberts, Atlanta, Ga.

The organization of the Council on Industrial Health will be perfected at a meeting to be held December 10, at which will be decided the plans for outlining the nature and the scope of the Council's activities. The creation of the Council on Industrial Health is another indication of the desire of the American Medical Association to do all that it can to promote the art and science of medicine and the betterment of the public health. It is, of course, confidently expected that the medical profession throughout the United States will support the work of the Council to the fullest possible extent.

STRAINS OF MENINGOCOCCI IN THE UNITED STATES

The meningococcus was recognized in 1887 as the cause of epidemic meningitis by Weichselbaum, who first identified this organism as a separate species. As late as 1909 it was still believed that there was no essential difference between individual members of the meningococcus group of organisms. In that year Dopter[1] discovered that some of the meningococci isolated from human beings could be distinguished from the ordinary type of organisms by agglutination reactions. Soon there were found to be a number of different subtypes of meningococci. In 1915 Gordon and Murray examined many strains of meningococci from cases occurring among British soldiers and found that all of them could be classified in four definite types: type I, type II, type III, type IV. For many years the National Institute of Health in Washington has received from persons throughout the United States numerous strains of meningococci. The strains thus received from January 1931 to March 1, 1937, have been typed according to the Gordon and Murray classification and analyzed by Branham and Carlin.[2] The typing was done by simple agglutination tests; absorption tests were not done, as they were not considered practical for routine purposes.

Meningococcic meningitis in the United States has returned in epidemic proportions about every ten years, ever since the first outbreak in Massachusetts in 1806. The year 1931, which was the first year in the period studied by Branham and Carlin, may be considered the end of an epidemic period, and the year 1935 represents a return of epidemic conditions. About 500 strains were typed. During the endemic years from 1932 to 1934, inclusive, the percentage of type II strains studied at the National Institute of Health rose from 4 in 1931 to 32 in 1932, remained high during the following year, and fell to 13.2 when epidemic conditions returned in 1935. The type II meningococcus during the last two epidemic waves in the United States has played an insignificant part; during the epidemics of the World War (1918-1919), however,

1. Zinsser, Hans, and Bayne-Jones, Stanhope: A Textbook of Bacteriology, ed. 7, New York, D. Appleton-Century Company, Inc., 1934, page 432.

2. Branham, Sara E., and Carlin, Sadie A.: A Study of Meningococci Recovered in the United States Since 1930, J. Bact. **34**: 275 (Sept.) 1937.

the type II meningococcus was abundant. Type IV during recent years seems to have dropped out of the picture altogether. The percentage of the I-III group of meningococci has greatly increased, and these strains accounted for the epidemics that occurred during the period under investigation. In the first year of the latest epidemic wave (1935) there were received at the institute about an equal number of type I and type III strains and strains that were designated as I-III because they were agglutinated equally well by the two type serums. In 1936 there was a trend in the serologic pattern toward type I and that trend was even more marked among the cultures received during the first two months of 1937.

Of the strains of meningococci typed from active cases in man during this period, 86 per cent fell into the I-III group. Of the total number of strains reported on, only twenty were known to have been isolated from the blood of patients, and sixteen, or 80 per cent of these, fell in the I-III group. Among 451 strains studied forty-two were from meningococcus carriers, and forty-one of these carrier strains were received during the spring of 1936. Among these forty-two carrier strains the type II organism prevailed. The type II meningococcus seems to have been relatively unimportant as a cause of epidemics in the United States during the last ten years.

Thus the meningococcus group of organisms is a heterogeneous group and the prevailing type occurring in epidemics in the United States changes from time to time. These facts may account in part for the difficulty of selecting the strains to be used in the preparation of therapeutic antimeningococcus serum.

HEREDITY AND THE NEUROPATHIC CONSTITUTION

Although there have been numerous inquiries into the incidence of psychoses and other "neuropathic" conditions among the relatives of the mentally defective, statistically valid figures as to frequency have not yet been obtained. According to a recent report,[1] 80 per cent of mental defectives have a positive family history of mental deficiency. This fact, if fact it is, lends support, it is asserted, to the theory that most mental deficiency is due to hereditary factors. In order to be significant, however, it must be controlled by knowledge also of the corresponding familial history of mental deficiency for the normal population. In an attempt to ascertain the frequency of such abnormalities among the relatives of normal persons, the Mental Deficiency Committee of the Royal Medico-Psychological Association devised a questionnaire, which was circulated among the mental hospitals, with the request that it be filled out by as many of the staff as possible. The form was arranged to insure anonymity. Four hundred and fifteen of 1,500 forms distributed were completed and returned. Of this number of persons who replied, 235 stated that they had one or more relatives with one or more of eleven "neuropathic" abnormalities. This figure corresponds to a frequency of 57 per cent. Although surprisingly high, there are several factors, the report states, disposing to give a falsely low figure: (1) the tendency of nurses with a bad family history to refuse to fill in the forms; (2) the fact that information was not asked about all possible relatives; (3) the fact that the inquiry did not include all conditions which might be considered to be of neuropathic importance.

A second question on which the forms gave some information was whether the so-called degenerative stocks are breeding faster than the more normal. Because of the difficulty in definition of "degenerative," this question may be approached statistically from a number of points of view. Five methods of approach were described in this report, none of which showed any significant difference between the abnormals and the normals. The committee was of the opinion, therefore, that there is no gross difference between the sizes of families in the normal and the abnormal groups.

This report raises several points of considerable interest, some of which have been recently pointed out by Myerson.[2] As a background for the study of the incidence of mental diseases, large segments of the normal population should be studied for a long time. Such a study cannot be done hurriedly. It involves more than the reading of records and the interviewing of relatives. It may require intensive studies by groups of people working together at least twenty years. Obviously these criteria have not been satisfied by the Mental Deficiency Committee report. In addition, there must be grave question as to the statistical significance of the material contained in the report when based on such a relatively small section of the population, a section moreover the completely representative neuropsychic qualities of which may be open to question. Furthermore, if only 415 out of 1,500 forms were returned, there arises the inevitable problem of not knowing what the other 1,085 forms would have shown had they been returned, and how these would have affected the percentages. This difficulty with the questionnaire and sampling method has been pointed out by numerous statisticians and has been referred to editorially on previous occasions. Thus, although no genuine attempt to extend knowledge should be condemned, it is obvious that the report in question adds but little to the factual information on the relative incidence of neuropathic conditions in the relatives of the normal.

1. An Inquiry into the Incidence of "Neuropathic" Conditions in the Relatives of Normal Persons, Report by Mental Deficiency Committee of the Royal Medico-Psychological Association, J. Ment. Sc. **83**: 247 (May) 1937.

2. Myerson, Abraham: Heredity and Mental Disease, Prev. Med. **7**: 135 (Sept.) 1937.

Current Comment

DEATHS FOLLOWING ELIXIR OF SULFANILAMIDE-MASSENGILL—V

In recent issues, THE JOURNAL has presented the tragic story of Elixir of Sulfanilamide-Massengill, particularly in reference to its scientific aspects.[1] Elsewhere in this issue [2] is the report of the field work and of the investigation of the S. E. Massengill Company by the United States government. The report points out that the number of deaths which have been confirmed is seventy-three (the number confirmed by the American Medical Association headquarters, as brought out in its last report) and that in addition twenty deaths followed administration of the elixir in which the exclusive responsibility of the drug has not yet been determined. The report brings out that the only test made of the elixir was that for flavor. The manufacturing formula given coincides very closely with the observations of the A. M. A. Chemical Laboratory. Of the 240 gallons manufactured, 228 gallons and 2 pints was seized by the federal Food and Drug inspectors. Eleven gallons and 6 pints was dispensed on prescription or over the counter sales. Of the latter quantity, about one half was consumed and caused the deaths; the other half was retrieved before consumption. In this interesting summary it is shown that the S. E. Massengill Company of Bristol, Tenn.-Va., sent out telegrams October 15 to withdraw the product from the market but that they were lamentably obscure as to the reason for withdrawal. The government insisted that a stronger telegram be sent, which was done October 19. The government, it is reported, is preparing citations asking that the S. E. Massengill Company show cause why it should not be subjected to criminal prosecution in the federal courts. In this connection the Secretary of Agriculture points out that in September 1934 and in March 1937 the S. E. Massengill Company was convicted and paid fines for violations of the Food and Drug Act (Notice of Judgment 23228 and Notice of Judgment 27136). Furthermore, the records of the Post Office Department show that in 1929 H. C. Watkins, the Massengill Company chemist who devised the elixir, was in the weight-reducing business in association with the Watkins Laboratories and others who were cited by the solicitor of the Post Office Department to show why a fraud order should not be issued. Mr. H. C. Watkins filed a stipulation with the department agreeing that the sale of the product would be abandoned and not resumed at any future time. The Secretary of Agriculture emphasizes the point made by THE JOURNAL that the fatal elixir was rushed on the market without adequate tests, despite previously published reports in the literature showing that diethylene glycol might be dangerous when taken internally. Other points emphasized both by THE JOURNAL and by the government are that the preparation was a semisecret one, that the presence of diethylene glycol was not disclosed and that no warning of danger appeared on the label. At present the most important factor is remedial legislative action. The recommendations made to Congress were the subject of editorial comment last week.[3] Since then a bill has been introduced in the Senate (S. 3073) by Senator Copeland, embodying essentially the recommendations of the Secretary of Agriculture. Certainly the public deserves protection from incompetent or callous manufacturers of drugs, whether the products are sold directly to the public as "patent medicines" or exploited to the medical profession.

1. Deaths Following Elixir of Sulfanilamide-Massengill, editorial, J. A. M. A. **109**: 1367 (Oct. 23), 1454 (Oct. 30), Elixir of Sulfanilamide-Massengill, ibid. **109**: 1531 (Nov. 6), 1724 (Nov. 20) 1937.

2. Deaths Due to Elixir of Sulfanilamide-Massengill, this issue, p. 1985.

3. Safeguards Proposed to Govern Distribution of Dangerous Drugs, editorial, J. A. M. A. **109**: 1911 (Dec. 4) 1937.

CRYSTALLINE VITAMIN A

One by one the many diverse substances of physiologic significance, e. g., hormones and vitamins, are yielding the secret of their structural configuration to the persistent investigations of the chemist. Not only has the isolation and identification of each substance been of theoretical significance, but the disclosure of chemical constitution has been of tremendous aid in suggesting physiologic functions and relationships, origin, fate, and methods of detecting and determining these compounds. The possible investigations concerned with a hormone or a vitamin invariably increase in number and expand in scope when isolation in pure form and establishment of structure are effected. In some instances, however, final crystallization of the physiologically active agent has eluded the combined efforts of many investigators principally because of the nonavailability of adequate concentrates or the lability of the compound. However, such circumstances, when encountered, have not greatly impaired the progress of studies designed to determine the physiologic significance and function. Indeed, in some instances, when actual isolation in crystalline form has been difficult to achieve, the chemical behavior has become known so thoroughly as to permit surprisingly accurate prediction of the chemical constitution. These comments are particularly applicable to vitamin A. Actual isolation of the vitamin itself in crystalline form appeared desirable chiefly for definite confirmation of the mass of circumstantial evidence pointing to its actual chemical configuration. This isolation has now been attained as a result of a series of noteworthy investigations at Oberlin College.[1] By the use of purified solvents, low temperatures and special technical precautions, it has been possible to isolate the vitamin in crystalline form from the liver oils of three different species of fish. Biologic assay indicates that the crystalline preparation has a value of approximately 3,000,000 international units per gram. The molecular weight determinations and elementary analyses of the compound correspond to a formula already suggested for the vitamin. Thus, a dietary essential which has been known for a quarter of a century has finally been obtained in a crystalline, probably pure, form. This constitutes another noteworthy achievement in the records of the isolation and identification of biologically important compounds.

1. Holmes, H. N., and Corbert, R. E.: J. Am. Chem. Soc. **59**: 2042 (Oct.) 1937.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARIZONA

Annual Registration Due January 1.—Every person practicing medicine, surgery or osteopathy in Arizona is required by law to pay annually on or before January 1, to the board of medical examiners, a renewal license fee of $3. Any licentiate who does not renew his license as required above is to be penalized $1 for each day that he practices without a renewal license, not to exceed $50. The board of medical examiners is to revoke the license of any licentiate who fails to renew his license for three successive years.

CALIFORNIA

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in California is required by law to register annually, on or before January 1, with the secretary-treasurer of the board of medical examiners and at that time to pay a fee of $2. Failure to pay the required fee within sixty days after January 1 works a revocation of a license, and thereafter a license may be reissued only after application and the payment of a $10 penalty.

Dr. Junius Harris Honored.—Dr. and Mrs. Junius B. Harris, Sacramento, were presented with a chest of silver at the third annual conference of county secretaries in San Francisco October 2, in appreciation of their efforts in conserving the interests of the medical profession. Dr. Harris has served as president of the Sacramento County Medical Society and of the California Medical Association and is now Vice President of the American Medical Association. He also served as a member of the House of Delegates of the American Medical Association in 1929, 1930, 1932 and 1934. Mrs. Harris has been active in the work of the Woman's Auxiliary.

Report on Medical Economic Survey.—*California and Western Medicine* announces that the "Formal Report on Factual Data" of the California medical-economic survey which was approved at the 1934 annual session of the California Medical Association has been completed. The study aimed to determine, among other things, the true incidence of sickness in the state. Paul A. Dodd, Ph.D., directed the study. The 224 page report may be purchased at $2 a copy. The state association expended more than $40,000 to defray part of the financial expense of the survey, while the Works Progress Administration and the Federal Emergency Relief Administration carried the balance of more than $55,000. The state department of health cooperated. The study covered 21,000 families, including almost 65,000 people in twenty-six representative counties of the state.

Annual Surgical Clinic.—Dr. John F. Erdmann, formerly professor of surgery, New York Post-Graduate Medical School, Columbia University, New York, was the guest of the Los Angeles Surgical Society at its annual meeting, December 10-11. Among the speakers at the afternoon sessions were:

Dr. Burns S. Chaffee, Long Beach, A Ruptured Appendix That Spontaneously Drained Through the Internal Abdominal Ring and Down the Canal of Nuck.
Dr. Albert J. Scholl, Los Angeles, Hemorrhagic Cyst of the Kidney.
Dr. Joseph Jellen, Los Angeles, Regional Ileitis.
Dr. Albert G. Bower, Los Angeles, The Administration of Sulfanilamide.
Dr. Vernon Thompson, Los Angeles, Treatment of Occlusive Vascular Diseases.
Dr. Wayland A. Morrison, Los Angeles, Solitary Paratyphoid Lesion of the Large Bowel.

The annual dinner was held December 10, at which Dr. Erdmann gave an illustrated address entitled "Curiosities in Surgical Practice."

COLORADO

Midwinter Clinics.—The Colorado State Medical Society will present the following guest speakers in clinics and formal addresses in its annual midwinter postgraduate clinics, December 15-17, at the Shirley-Savoy Hotel, Denver:

Dr. Albert J. Brown, Omaha, tumor clinic; Treatment of Diseases of the Stomach.
Dr. Herman L. Kretschmer, Chicago, clinic on prostatic obstruction; Tumors of the Kidney.
Dr. A. Graeme Mitchell, Cincinnati, clinic on nephritis; What I Don't Know About Endocrinology.
Dr. Robert D. Schrock, Omaha, fracture clinic; Fractures of the Lower End of the Radius and Ulna.
Dr. Don C. Sutton, Chicago, clinic on arteriosclerosis; Obscure Fevers.

Colorado physicians will also present papers and conduct clinics. A stag smoker will be held Wednesday evening and the banquet Friday evening. The woman's auxiliary to the Medical Society of the City and County of Denver is planning entertainment for the visiting ladies.

FLORIDA

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in Florida is required by law to register annually on or before January 1, with the secretary of the state board of health, and at that time to pay a fee of $1. A licentiate failing to register annually is liable to a fine of not more than $50.

Society News.—Dr. Walter C. Jones Jr., Miami, was elected president of the Florida East Coast Medical Association at its tenth annual convention, in Hollywood, November 12-13; Drs. Elbert McLaury, Hollywood, and John Randolph Perdue, Miami Beach, were named vice presidents, and Dr. Thomas C. Kenaston, Cocoa, secretary-treasurer.——The fall meeting of the Florida Midland Medical Society was addressed in St. Petersburg, October 28, among others, by Drs. Thomas C. Maguire, Plant City, on "Congenital Abnormalities of the Intestinal Tract"; Martin H. Stuart, St. Petersburg, "A Palliative Treatment of Acute Mastoiditis," and Harold C. McDowell, Venice, "Bone Graft of the Neck of the Femur."

GEORGIA

State Pediatric Meeting.—The fifth annual scientific meeting of the Georgia Pediatric Society was held in Atlanta, December 9, with the following speakers:

Dr. Joseph Brennemann, Chicago, Acute Laryngotracheobronchitis; The Acute Abdomen in Childhood.
Dr. Ralph S. Muckenfuss, New York, Immunization Against Common Infections of Childhood; Virus Infections of the Central Nervous System.
Dr. Priscilla White, Boston, Endocrine Problems in Juvenile Diabetes; Recent Problems in Juvenile Diabetes.
Dr. Paul H. Holinger, Chicago, Bronchial Obstruction in Infancy; Atelectasis and Bronchiectasis.

Dr. Henry Clifford Sauls, Atlanta, president of the Fulton County Medical Society, gave the address of welcome.

ILLINOIS

Number of Insane Patients Doubles in Twenty-Five Years.—The number of insane persons in state institutions in Illinois has doubled in the last twenty-five years, according to a report of the state department of public welfare. The commitments have increased 16⅔ per cent during the last five years. At the same time the number of epileptic and feebleminded persons cared for by the state has increased nearly five times over a twenty-five year period and commitments to penal institutions are 11,578 for 1937 as of October 1 as compared with 3,276 in 1912. The steady increase has been most noticeable during the ten year period between 1927 and October 1 of this year. In 1927 there were 20,540 insane persons committed to institutions in Illinois, and October 1 the total stood at 28,715; in 1912 the number of insane in state institutions was 14,426. In 1912 there were 1,479 feebleminded and epileptic persons cared for by the state, while in 1927 this number had increased to 4,562 and at the time of the report this year it reached 6,995. Delinquents committed by the state show a smaller increase over the twenty-five year period. In 1912 there were 956 delinquents cared for, in 1927 there were 1,217 and this year the number had decreased to 1,004. The state department of public welfare was caring for 51,275 persons October 1. In 1912 the number was 25,385 and in 1927 15,644.

Chicago

Society News.—At a meeting of the Society of Medical History of Chicago, November 30, Drs. Clarence A. Earle, Des Plaines, Ill., discussed "Pioneer Medicine" and William Allen Pusey, "Giants of Medicine in Pioneer Kentucky."——The Chicago Orthopaedic Society was addressed December 10, among others, by Dr. Ralph K. Ghormley, Rochester, Minn., on "Some Unusual Lesions of Vertebrae."

The Patterson Institute for Cancer Research.—A fund of more than $500,000 has been established for cancer research and investigation, the income of which will be used in Passavant Hospital. The institute will be known as the Patterson Institute for Cancer Research. Miss Edith Patterson, Sterling, Ill., is the donor in memory of her brother, Floyd Elroy Patterson, who died in 1928. Under the terms of the agreement between

Miss Patterson, Northwestern University and the hospital, the building occupied by the Passavant Hospital will be named the Floyd Elroy Patterson Building, although the unit will continue to be known as the Passavant Hospital, it was announced. The institute will be organized as a department of the hospital with a yearly appropriation of $12,000 for treatment and research.

LOUISIANA

Personal.—Dr. Lucien A. Ledoux, New Orleans, has been appointed associate professor of gynecology at Louisiana State University Medical Center, New Orleans, it is reported.

Society News.—At a meeting of the Ouachita Parish Medical Society in Monroe, November 4, the speakers were Drs. Edgar Hull and Joseph O. Weilbaecher Sr., both of New Orleans; their subjects were "Nutritional Factors in Cardiac Failure" and "The New Insulin Therapy in Diabetic Disease; Namely, Protamine Zinc Insulin," respectively.

Annual Renewal Due January 1—Every practitioner of medicine and surgery holding a certificate to practice in Louisiana is required by law to have his certificate renewed annually, on or before January 1, by the secretary-treasurer of the state board of medical examiners and at that time to pay a fee of $2. The board may by unanimous vote revoke any certificate not renewed.

MAINE

Society News.—The Portland Medical Club was addressed October 5 by Dr. Roderick L. Huntress on "Some Causes of Urgency and Frequency Without Urethral Obstruction."——At a meeting of the Kennebec County Medical Association in Gardiner, October 27, the speakers included Dr. Henry H. Faxon, Boston, on "Vascular Diseases."——Dr. Richard B. Cattell, Boston, addressed the Oxford County Medical Association in Bethel, October 26, on "Surgical Diseases of the Colon and Rectum."——At a meeting of the Washington County Medical Society in East Machias, October 8, Dr. Laforest J. Wright, Bangor, spoke on "The County Society: Its Function and Value to Members"; Dr. Magnus F. Ridlon, Bangor, "Carcinoma of the Uterus," and Ralph W. Wakefield, Bar Harbor, malpractice. Dr. Wakefield addressed the fall meeting of the York County Medical Society in Kennebunk, October 6; a symposium on obstetrics was also presented by Drs. Roland B. Moore, Portland; Chester F. McGill, Portsmouth, N. H., and Thomas A. Foster, Portland.

MICHIGAN

New Health Association Officers.—Dr. Carleton Dean, Charlevoix, director, district health department, Children's Fund of Michigan, was elected president of the Michigan Public Health Association at its seventeenth annual conference in Lansing November 11. He succeeds Dr. Jacob D. Brook, Grand Rapids, health officer of Kent County, who was named to the board of directors. Dr. John L. Lavan, health officer of Grand Rapids, was elected vice president, and Marjorie Delavan, Lansing, director of the bureau of education, state department of health, was made secretary-treasurer.

Occupational Diseases Made Reportable.—A law requiring every physician, hospital superintendent or clinic registrar having knowledge of a case of occupational disease to report it within ten days to the state department of health went into effect October 29, according to the state medical journal. The law describes the characteristics of occupational diseases and empowers the state department of health to provide employers with the proper instruction and information to prevent these diseases.

Symposium on Occupational Disease.—The Michigan Department of Labor and Industry sponsored a symposium on occupational disease at the Detroit-Leland Hotel, Detroit, October 21-22. Speakers included:

Dr. Anthony J. Lanza, New York, Social Aspect of Occupational Diseases.
Dr. John T. Murphy, Toledo, Ohio, Radiologic Aspects of Silicosis.
Philip Drinker, Ch.E., Boston, Industrial Dust Hazards and Their Control.
Dr. Joseph C. Aub, Boston, Lead Poisoning.
Dr. William D. McNally, Chicago, Poisons Under an Occupational Disease Act.

Graduate Conferences on Tuberculosis.—The Wayne County Medical Society, the Detroit Department of Health and the Detroit Tuberculosis Sanatorium cooperated in the fall graduate conferences, which this year were devoted entirely to tuberculosis. The series of lectures and demonstrations, held at weekly intervals, opened October 27 with Dr. Kendall Emerson, New York, as the speaker on "Present Trend of Tuberculosis." Other speakers included:

Dr. Esmond R. Long, Philadelphia, Importance of Protecting the Child and the Young Person Against Tuberculosis.
Dr. James N. Baker, Montgomery, Ala., The Role of the Private Physician in Tuberculosis Case Finding.
Dr. John B. Hawes II, Boston, The Care of the Patient After the Sanatorium.
Dr. Don M. Griswold, Albany, N. Y., Factors in the Control of Tuberculosis.
Dr. George G. Ornstein, New York, The Pathogenesis of Pulmonary Tuberculosis from the Physician's Point of View.

MINNESOTA

Fined for Selling Contraceptives.—Mrs. Cecilia Scott pleaded guilty in the district court of Hennepin County at Minneapolis November 22 to a charge of the unlawful sale of contraceptives. She was sentenced to serve sixty days in the Minneapolis Work House or pay a fine of $75; she paid the fine. Mrs. Scott stated that she came to Minneapolis in the spring of 1937 from Kansas City, Mo.; that she represented the Smith Laboratory Corporation, and that they had an office at 408 Wesley Temple Building. According to the state board of medical examiners, Mrs. Scott did not confine her contacts to the medical profession but went to private homes because of information that she obtained through the daily birth notices in the Minneapolis newspapers. When policewomen called on Mrs. Scott they were told, among other things, that a physical examination could be arranged for them at the office of Arthur Kolling, a chiropractor in Minneapolis. Kolling has no license to practice medicine in Minnesota and already has been convicted of practicing illegally.

NEW YORK

Annual Registration Due January 1.—Every practitioner of medicine and surgery in New York is required by law to apply annually, on or before January 1, to the secretary of the board of medical examiners for a certificate of registration, on application forms furnished by him, and to pay at that time a fee of $2. The law authorizes the secretary of the board to permit secretaries of duly incorporated medical societies to act as his representatives, to receive and transmit to him such applications and fees. Practitioners are liable to severe penalties for failing to register and for continuing in practice thereafter.

Staphylococcic Food Poisoning.—About forty cases of food poisoning attributed to the eating of chocolate éclairs were recently reported to the state department of health from Newburgh and Orange County. All the éclairs were from a single batch prepared at a local bakery during the night of October 22 and sold October 23. The éclairs were made by the pastry baker without any assistance, but two other persons were in the bakery during the night. One admitted having had a sty which had disappeared two days before. It was found also that a sty developed in another employee of the bakery October 24. The state laboratory reported that staphylococci were found in great numbers in the éclairs.

New York City

Third Harvey Lecture.—Dr. Cecil K. Drinker, professor of physiology, Harvard University School of Public Health, Boston, will deliver the third Harvey Lecture of the current series at the New York Academy of Medicine, December 16. Dr. Drinker will speak on "The Functional Significance of the Lymphatic System."

Society News.—George R. Cowgill, Ph.D., New Haven, Conn., and Dr. Richard Bauer, Vienna, Austria, addressed the Medical Society of the County of Kings, November 16, on "Vitamin Requirements and the Clinics" and "Diagnosis of Diseases of the Liver" respectively.——Dr. Charles R. Stockard, professor of anatomy, Cornell University Medical College, delivered the first and second Joseph Collins Lectures at the New York Academy of Medicine, December 2, on "The Mechanisms Operating the Body as an Integrated Unit" and December 8, "Endocrine Changes and Modifications in Function and Behavior." A symposium on tumors of childhood was presented at a meeting of the section of pediatrics of the academy, December 9, by Drs. Bradley L. Coley, George T. Pack, Hayes E. Martin, William L. Watson and Lloyd F. Craver.

Dr. Levene to Receive Nichols Medal.—Dr. Phoebus Aaron Theodore Levene, member of the Rockefeller Institute for Medical Research since 1907, will receive the William H. Nichols Medal of the New York Section of the American Chemical Society at a meeting March 12, 1938, it was recently announced. Dr. Levene is honored "for his study of the configurational relationships of the simpler optically active organic

compounds." He is the author of papers on proteins, nucleins, carbohydrates, lipoids and problems of stereochemistry and of two monographs entitled "Hexosamines and Mucoproteins" and "Nucleic Acids." Dr. Levene was graduated in medicine in Russia in 1891 and came to America in 1893. After a period of practicing medicine, he began research in biologic chemistry and in the next few years was associate in chemistry at the New York Pathological Institute.

Pharmacologist Honored.—Friends, students and alumni of New York University College of Medicine presented to the college an oil portrait of Dr. George B. Wallace, professor of pharmacology, on his completion of thirty-six years of teaching November 15. Dr. Alfred N. Richards, professor of pharmacology, University of Pennsylvania School of Medicine, Philadelphia, made the presentation speech and the portrait was accepted by Dr. Currier L. McEwen, dean of the college. Dr. Wallace, who is 63 years old, graduated from the University of Michigan Department of Medicine and Surgery, Ann Arbor, in 1897. He is a member of many scientific societies, a founder of several and has served as president of the American Society of Pharmacology and Experimental Therapeutics, the Harvey Society and the Society of Experimental Biology and Medicine. He is chairman of the committee on pharmacology and drugs of the 1939 World's Fair.

Hospital News.—The Max and Flora Einhorn Memorial Building of the Lenox Hill Hospital was dedicated October 22. The building, erected at a cost of $400,000, is the gift of Dr. Einhorn, who has been associated with the hospital for many years. It contains a twenty-five bed pavilion, an auditorium, a roof garden, a hydrotherapy department and a swimming pool.——The new Central Nurses' Residence on Welfare Island, which will make possible the evacuation of unsuitable quarters at several city institutions, has recently been completed. Built on a loan and grant agreement with the Public Works Administration at a cost of $1,500,000, the new residence will provide 678 rooms. The department of hospitals recently announced that a residence with 669 rooms is being completed at Kings County Hospital, Brooklyn. Homes for nurses have also been built at Greenpoint, Kingston Avenue and Queens General hospitals, and extensions have been added at other hospitals. There are now 2,189 rooms in which nurses may live under satisfactory conditions, the announcement stated.——A new building for the Bronx Eye and Ear Infirmary, recently completed at a cost of $500,000, was opened without ceremony October 15.

NORTH CAROLINA

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in North Dakota is required by law to register annually on or before January 1, with the secretary-treasurer of the board of medical examiners, and at that time to pay a fee of $5 if a resident of North Dakota or $2 if a nonresident. A practitioner may not lawfully practice if he has not registered. If he does so his license may be revoked and can be reinstated on the payment of unpaid fees and 50 cents for each month of default.

Special Society Meetings.—The North Carolina Eye, Ear, Nose and Throat Society held its annual meeting in Charlotte, November 20, with the following guest speakers: Drs. Leroy A. Schall, Boston, on "Laryngectomy—Its Place in the Treatment of Cancer of the Larynx"; Wilfred E. Fry, Philadelphia, "Ocular Pathology Associated with Increased Intracranial Tension" and Gabriel Tucker, Philadelphia, "Gastroscopy for Diagnosis and Foreign Body Removal."——At a quarterly meeting of the North Carolina Neuropsychiatric Society in Asheville, October 29, Dr. David C. Wilson, Charlottesville, Va., discussed a case of neuroblastoma with Hutchinson's syndrome and Dr. S. Spafford Ackerly, Louisville, Ky., a case of absence of corpus callosum confused with psychopathic personality. Dr. James K. Hall, Richmond, delivered an address in the evening on "Psychiatry in Retrospect and Prospect."——The North Carolina Radiological Society met in Raleigh November 11 with Dr. Frank E. Adair, New York, as guest speaker at an evening banquet with the Wake County Medical Society, on "Radiation and Surgical Treatment of Breast Cancer."

OKLAHOMA

Personal—Dr. James A. Land, Hobart, has been appointed medical superintendent of the Western Oklahoma Tuberculosis Sanatorium, Clinton, to succeed Dr. Will C. Wait, who will enter practice in McAlester.——Dr. Shade D. Neely, Muskogee, has been appointed health superintendent of Muskogee County to succeed Dr. Charles E. White, Muskogee, and Dr. Gappa M. Rushing, Durant, in Bryan County to succeed Dr. Henry B. Fuston, Bochito.——Dr. George W. Baker, Walters, has been appointed health superintendent of Cotton County and Dr. Jessie M. Harris, Wilburton, of Latimer County.

Society News.—At a meeting of the Okmulgee-Okfuskee County Medical Society, Henryetta, October 25, the speakers, all of Tulsa, were Drs. Morris B. Lhevine, "Diagnosis and Treatment of Carcinoma of the Breast"; Andre B. Carney, "Surgical Procedures Following Irradiation in Carcinoma of the Breast" and Russell C. Pigford, "Legislative Measures Affecting the Medical Profession in Oklahoma."——Dr. Martin R. Beyer, Oklahoma City, addressed the Tulsa County Medical Society, Tulsa, November 8, on undulant fever.

PENNSYLVANIA

Personal.—Dr. Robert C. Hughes, Paoli, was elected coroner of Chester County at the recent election.——Dr. Dale E. Cary, Lancaster, was elected mayor of the town.——Dr. Horace V. Pike retired November 15 as clinical director of the Danville State Hospital after eighteen years as a member of the staff.

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in Pennsylvania is required by law to register annually, on or before January 1, with the board of medical education and licensure in the department of public instruction, and to pay a fee of $1 or such fee as may be fixed by the department of public instruction. A practitioner who fails to register and who continues to practice is liable to a fine of from $10 to $100.

Philadelphia

Society News.—Dr. Seth A. Brumm, among others, addressed the Pennsylvania State Physical Therapy Association, November 18, on "Electrocoagulation of Tonsils."——Dr. Wilhelm C. Hueper, Wilmington, Del., addressed the Philadelphia Urological Society, November 22, on "Experimental Production of Bladder Tumors in Animals."——Dr. Edward D. Churchill, Boston, delivered the Mütter Lecture of the College of Physicians of Philadelphia, December 1, on "The Pathology and Surgery of Bronchiectasis."——Dr. Nathaniel S. Yawger, among others, addressed the Philadelphia Neurological Society, November 19, on "Marihuana: Our New Addiction."

Symposium on Biophysics.—The American Institute of Physics in cooperation with the Eldridge Reeves Johnson Foundation for Medical Physics at the University of Pennsylvania sponsored a symposium on biophysics November 4-6. Among those who appeared on the program were:

Detlev W. Bronk, Ph.D., director of the Johnson Foundation, The Relation of Physics to the Biological Sciences.
Edmund Newton Harvey, Ph.D., Princeton, N. J., The Physical Properties of Protoplasm.
Dr. Herbert S. Gasser, New York, Electrical Signs of Biological Activities.
Wendell M. Stanley, Ph.D., Princeton, N. J., The Biophysics and Biochemistry of Viruses.
Wallace O. Fenn, Ph.D., Rochester, N. Y., The Mechanics of Muscular Contraction.

Irving Langmuir, Ph.D., director of research, General Electric Company, Schenectady, delivered the Johnson Foundation Lectures November 4 and 5, on "Monolayers and Multilayers and Their Applications to Biological Problems."

Pittsburgh

"Scientific Day" at Montefiore Hospital.—Dr. Irving Sherwood Wright, New York, was the guest speaker at the annual "Scientific Day" of Montefiore Hospital, November 20, addressing an evening meeting on "A Critical Analysis of Recent Advances in the Study of Vascular Disease." In the morning the department of ophthalmology gave a demonstration of eyegrounds in arteriosclerosis and hypertension, followed by discussions as follows: Drs. Verner B. Callomon, on "Bronchial Tumor with Atelectasis"; Meyer A. Rosenbloom, "Sarcomatosis of Stomach with Metastasis to the Heart"; Yale D. Koskoff, "Ligation of Carotid Artery for Intracranial Bruit," and Harry I. Miller, "Peripheral Vascular Disease."

SOUTH CAROLINA

Society News.—Drs. Jefferson C. Pennington, Nashville, Tenn., and Edgar G. Ballenger, Atlanta, Ga., were the guest speakers at the annual meeting of the South Carolina Urological Association in Columbia, October 13, on "Management of Calculi in the Upper Urinary Tract" and "Management of Tumors of the Bladder, Both Benign and Malignant" respectively.——Dr. Irvin Abell, Louisville, Ky., President-Elect of the American Medical Association, was the guest of the Columbia Medical Society, November 8, speaking on "The Relation of Diabetes to Surgery." Dr. Foster M. Routh discussed "The

Leukopenic Index in Food Allergy."——Dr. Joseph D. Guess, Greenville, addressed the Anderson County Medical Society, Anderson, October 13, on "Problems in the Management of Labor."

TENNESSEE

Personal.—Dr. Monroe F. Brown, Fayetteville, has succeeded Dr. Frank L. Roberts as health officer of Gibson County with headquarters in Trenton. Dr. Roberts is now professor of preventive medicine at the University of Tennessee College of Medicine, Memphis.

Nobel Prize Winner to Give Flexner Lectures.—Dr. Albert Szent-Györgyi, professor of medical chemistry in the Royal Hungarian Franz Joseph University, Szeged, Hungary, who received the Nobel Prize in Medicine for 1937, has been chosen to give the Flexner Lectures at Vanderbilt University School of Medicine, Nashville, for the session of 1938-1939.

Society News.—At a meeting of the Dyer, Lake and Crockett Counties Medical Society in Dyersburg, November 3, the speakers were Drs. Robert Lyle Motley, Memphis, on "Treatment of Cardiac Decompensation and Edema"; Duane M. Carr, Memphis, "Pneumonia," and William P. Watson, Dyersburg, "Accidents During Labor."——A symposium on gallbladder disease was presented before the Memphis and Shelby County Medical Society, Memphis, October 5, by Drs. Henry G. Rudner, Joseph A. Crisler Jr. and Lucius C. Sanders. Drs. W. Likely Simpson and William S. Anderson, Memphis, addressed the society, October 19, on "Foreign Bodies in the Air and Food Passages" and "Indications for Hysterectomy and Radium in Uterine Fibroids" respectively.

University News.—Dr. Harry A. Davis, instructor in pathology, George Washington University School of Medicine, Washington, D. C., is serving as acting associate professor of pathology at the University of Tennessee College of Medicine, Memphis, in the place of Dr. Walter W. Brandes, who is on leave of absence because of illness. William R. Amberson, Ph.D., recently resigned as head of the department of physiology to become professor of physiology at the University of Maryland School of Medicine, Baltimore. His successor has not been appointed. Dietrich C. Smith, Ph.D., instructor in physiology, also went to Maryland as associate professor.

TEXAS

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in Texas is required by law to register annually on or before January 1, with the state board of medical examiners, and at that time to pay a fee of $2. If a practitioner fails to renew his registration within sixty days after January 1, his license is suspended.

Society News.—Drs. Henry G. Poncher and Arthur H. Parmelee, Chicago, were the guest speakers at a meeting of the Texas Pediatric Society in Dallas, October 23. Dr. Poncher spoke on "Problems in Nutrition—Vitamins" and "Upper Respiratory Infections" and Dr. Parmelee on "Congenital Syphilis" and "Conditions in the New-Born."——Drs. Henry M. Winans and Robert F. Short Jr., Dallas, addressed the Grayson County Medical Society in Sherman, October 12, on "Diagnosis of Upper Quadrant Lesions" and "Surgery of Upper Quadrant Lesions" respectively.——Dr. Louis F. Knoepp, Beaumont, addressed the Hardin-Tyler Counties Medical Society, October 12, in Kountze on "Surgical Lesions in Tuberculosis."——Dr. French K. Hansel, St. Louis, addressed the Dallas Academy of Ophthalmology and Otolaryngology in October on "Etiology and Treatment of Rhinitis."——Dr. Edward P. Leeper, Dallas, discussed "Heart Disease Due to Vitamin Deficiency" before the Dallas Heart Association, November 1.——Drs. J. C. Alexander and Milford O. Rouse, Dallas, addressed the Ellis County Medical Society, Waxahachie, October 13, on "Sulfanilamide as a Urinary Antiseptic" and "Diarrheas" respectively.——Drs. George D. Mahon and Charles L. Martin, Dallas, addressed the Potter County Medical Society, Amarillo, October 11, on "Resection of the Right Half of the Colon" and "Treatment of Advanced Cancer" respectively.

WASHINGTON

Society News.—At a meeting of the Washington State Obstetrical Association in Spokane October 2 there were discussions of "Induction of Labor," "Analgesia and Anesthesia," and "What Is of Most Importance in Obstetrics Today." Dr. Henry H. Skinner, Yakima, is president of the association and Dr. Philip C. Kyle, Tacoma, secretary.——Dr. Henry S. Atwood, Yakima, addressed the Yakima Valley Medical Society in Yakima, October 11, on "Spinal Anesthesia."——Drs. John G. Cheetham and Leo J. Meienberg, Portland, Ore., addressed the Cowlitz County Medical Society, Longview, October 13, on sulfanilamide treatment of gonorrhea.——Dr. Frederick Lemere, Seattle, addressed the Pierce County Medical Society, Tacoma, October 12, on "Insulin Shock in Treatment of Psychosis."——At the first fall meeting of the Walla Walla Valley Medical Society, Walla Walla, October 14, Drs. Frank B. Kistner and Robert L. Benson, Portland, discussed "Asthma and Hay Fever as Related to Paranasal Sinus Infection."

WEST VIRGINIA

Public Health Meeting.—Dr. Reece M. Pedicord, Wheeling, was elected president of the West Virginia Public Health Association at its annual meeting in Charleston November 7-9. Drs. Charles E. Watkins, Fayetteville, and William W. Hume, Beckley, were elected vice presidents and Dr. Thomas W. Nale, Charleston, secretary. Among the guest speakers at the meeting were Drs. Reginald M. Atwater, secretary of the American Public Health Association, New York, on "Today's Trends in Public Health"; Halbert L. Dunn, chief statistician for vital statistics of the Bureau of the Census, Washington, D. C., "Complete Birth Registration," and Anthony J. Lanza, New York, "The New Day in Disease Control and Prevention Through Industrial Hygiene."

WISCONSIN

Society News.—Speakers before the Milwaukee Society of Clinical Surgery, November 23, were Drs. Edmund W. Schacht, Racine, on "Carcinoma of the Scrotum" and Charles B. Huggins, Chicago, "What Is the Function of the Arterial Supply of the Liver?"——Dr. Oscar A. Sander, Milwaukee, addressed the University of Wisconsin Medical Society, Madison, November 23, on silicosis.——Dr. Roy P. Potter, Marshfield, addressed the Columbia-Marquette-Adams County Medical Society, Adams, November 9, on "Diseases of the Chest."

District Meeting.—The annual meeting of the Fifth District of the state medical society was held in Two Rivers, October 14, with the following guest speakers: Drs. Nelson M. Barker, Rochester, Minn., on hypertension; Harry L. Smith, Rochester, diagnosis and treatment of carotid sinus syncope; William S. Middleton, Madison, newer therapy of lobar pneumonia, and David A. Cleveland, Milwaukee, spinal and cerebral injuries. Dr. James C. Sargent, Milwaukee, president of the state medical society, discussed society plans for the coming year.

Committee to Study Sickness Care.—At the recent annual meeting of the Medical Society of Wisconsin a special committee was appointed to investigate the adequacy of sickness care in the state. Dr. Raymond G. Arveson, Frederic, is chairman and the other members are Drs. Henry J. Gramling and Robert W. Blumenthal, Milwaukee; Joe Newton Sisk, Madison, and Henry H. Christofferson, Colby. It is planned that the committee shall hold hearings in various parts of the state to receive complaints, opinions and recommendations of all persons in certain key centers who are familiar with the broad problem of sickness care.

PUERTO RICO

The Annual Medical Meeting.—The thirty-fourth annual session of the Puerto Rico Medical Association will be held at the association headquarters in Santurce, December 17-19. Special guests will be Drs. Ramon Castroviejo and Dana Winslow Atchley, New York, who will conduct clinics and give addresses on "The Present Status of Ophthalmic Surgery" and "Nephrosis and the Nephrotic Syndrome" respectively. Among others on the program will be:

Dr. Manuel E. Pujadas Diaz, Santurce, Celiac Disease.
Dr. Oscar G. Costa-Mandry, Santurce, Study of Food Infections in Puerto Rico.
Dr. Rafael Lopez Nussa, Santurce, Surgery of the Sympathetic.
Dr. A. Rodríguez Olleros, Madrid, Spain, Gastroscopy.
Drs. Luis J. and Ricardo Fernández, San Juan, Treatment of Gonococcic Ophthalmia with Sulfanilamide.
Dr. Ezequiel Martínez-Rivera, Rio Piedras, Venereal Disease from the Public Health Point of View.
Dr. Carlos González, Mayagüez, Therapeutic Use of Sulfanilamide in Infections of Streptococcic Origin.

A feature of the meeting will be three showings of the film "Diagnosis of Syphilis," prepared by the American Medical Association and the U. S. Public Health Service. The scientific sessions will be held in the afternoons and evenings; mornings will be devoted to clinics at various hospitals.

GENERAL

New Journal of Neurophysiology.—Announcement is made of the forthcoming publication of the *Journal of Neurophysiology* under an editorial board consisting of Drs. Joannes G. Dusser de Barenne and John F. Fulton, Sterling professors of physiology, Yale University School of Medicine, New Haven, Conn., and Ralph W. Gerard, associate professor of physiology, University of Chicago. The aim of the new journal is to serve as a channel for prompt publication of original work bearing on the functions of the nervous system, peripheral and central. The publisher is Charles C. Thomas, Springfield, Ill.

Y. M. C. A. to Cooperate in Syphilis Campaign.—The National Council of the Young Men's Christian Association has issued a bulletin urging local units to cooperate with physicians and health officials in the campaign against syphilis. The local units are urged to begin at once to (1) investigate local conditions, the prevalence of the disease and available treatment, (2) appoint committees to consider effective ways and means of aiding local medical and public health authorities, (3) hold social hygiene meetings at which syphilis is the subject for discussion, and (4) arrange with physicians for the taking of Wassermann tests in Y. M. C. A.'s where practicable. It is estimated that 75 per cent of the association's members are between 11 and 30 years of age, the age group in which the public health service reports that more than half the primary syphilitic infections occur.

Conference on Maternal and Child Welfare.—Miss Katharine F. Lenroot, chief of the Children's Bureau, U. S. Department of Labor, has called a conference on "Better Care for Mothers and Babies" to be held in Washington, D. C., January 17-18. A planning committee for the conference has been appointed with Mrs. J. K. Pettengill, Detroit, president of the National Congress of Parents and Teachers, as chairman; Dr. Fred L. Adair, Chicago, chairman of the American Committee on Maternal Welfare, as vice chairman, and Mrs. Nathan Straus, New York, representing the National Council of Jewish Women, as secretary. The planning committee will represent numerous organizations in the field of health and welfare. Plans for the conference grew out of findings presented to the Children's Bureau by its advisory committee on maternal care, of which Dr. Adair is chairman, the announcement stated.

Advisory Committee on Pneumonia.—An advisory committee, recently appointed by Dr. Thomas Parran, surgeon general, U. S. Public Health Service, to plan a program for pneumonia control on a national scale, held its first meeting November 12, in Washington. Members of the committee are:

Dr. Donald B. Armstrong, third vice president, Metropolitan Life Insurance Company, New York.
Dr. David P. Barr, Busch professor of medicine, Washington University School of Medicine, St. Louis.
Dr. Russell L. Cecil, professor of clinical medicine, Cornell University Medical School, New York.
Dr. Lloyd D. Felton, associate in pathology and bacteriology, Johns Hopkins University School of Medicine, Baltimore.
Dr. Alfred Friedlander, dean and professor of medicine, University of Cincinnati College of Medicine.
Dr. Roderick Heffron, Commonwealth Fund, New York.
Dr. Ernest E. Irons, clinical professor of medicine, Rush Medical College, Chicago.
Dr. Roger I. Lee, consultant in internal medicine, Boston.
Dr. George H. Ramsey, assistant commissioner for preventable diseases, State Department of Health, Albany, N. Y.

National Foundation for Infantile Paralysis.—President Roosevelt announced November 24 appointment of thirty-four citizens of various parts of the United States to serve as trustees of the new National Foundation for Infantile Paralysis now in process of formation. According to a statement by the President when he announced the new foundation recently, its general purpose will be "to lead, direct and unify the fight on every phase of this sickness." It is hoped that a fund of from $7,000,000 to $10,000,000 will be raised in the next five years. With this the foundation "will make every effort to ensure that every responsible research agency in this country is adequately financed to carry on investigations into the cause of infantile paralysis and the methods by which it may be prevented." It also aims to develop means of enabling those already crippled by the disease to become economically independent in their own communities. The first task of the foundation will be to arrange the fifth annual "birthday balls" to be held January 29 in honor of the President's birthday, which is January 30. This year all funds from the celebration will be given to the new foundation, instead of being divided as heretofore between the Georgia Warm Springs Foundation and local communities. The newly appointed trustees are: Cornelius N. Bliss, John S. Burke, Carle C. Conway, James V. Forrestal, S. Parker Gilbert, W. Averell Harriman, Jeremiah Milbank, Keith Morgan, Thomas E. Murray Jr., Basil O'Connor, Edward Stettinius Jr., Thomas J. Watson and Clarence Woolley, all of New York; George E. Allen, Commissioner of the District of Columbia; Robert V. Fleming, Washington; James F. Bell, Minneapolis; William L. Clayton, Houston, Texas; Robert H. Colley, Philadelphia; Harvey C. Couch, Pine Bluff, Ark.; Walter J. Cummings, Marshall Field and Walter P. Murphy, Chicago; Fred J. Fisher, Detroit; Edsel B. Ford, Dearborn, Mich.; Elton Hoyt 2d, Cleveland; William F. Humphrey, San Francisco; John R. Macomber, Boston; Leighton McCarthy, Toronto; Robert E. McMath, Bethlehem, Pa.; Carroll B. Merriam, Topeka, Kan.; Charles E. Perkins, Santa Barbara, Calif.; George Rand, Buffalo; Robert W. Woodruff, Atlanta, Ga., and S. Clay Williams, Winston-Salem, N. C.

FOREIGN

Typhoid in London Suburb.—The New York *Times* reported November 22 that 137 cases of typhoid had occurred in the preceding fortnight in Croydon, a suburb of London, said to have modern water, drainage and health services. Seven deaths had occurred up to November 20. Tests showed that Croydon's water services had "the highest standard of bacterial purity," the *Times* reported.

CORRECTIONS

International Unit for Estrone.—On page 1865 of the December 4 issue of THE JOURNAL, in the article by R. T. Frank and others, the international unit for estrone (theelin, "ketohydroxyestrin") should have been given as 0.1 microgram instead of 1 microgram.

Duration of Immunity Against Diphtheria.—In THE JOURNAL, November 20, page 1684, in the first column, second line, following the word "negative," the following sentence should have appeared in the discussion by Dr. M. Bernard Brahdy of the paper by Dr. William H. Park: "For the results with precipitated toxoid I am going to present data obtained by Dr. O'Brien in a group of infants who had no previous injection of antigen."

Government Services

Examination for Appointment in the Navy

Announcement is made of an examination for appointment as lieutenant (junior grade) in the medical corps of the U. S. Navy to be held at all naval hospitals in the United States and at the Naval Medical School, Washington, D. C., beginning May 16, 1938. Candidates must be between 21 and 32 years old at the time of appointment, must be graduates of class A medical schools and must have completed an internship of one year in a hospital accredited for interns by the American Medical Association and the American College of Surgeons. Those who are interested should write to the Surgeon General, U. S. Navy, Bureau of Medicine and Surgery, Navy Department, Washington, D. C., for further information concerning the examination and the procedure to follow for appearance before the examining boards.

Biochemist Wanted for Research on Syphilis

The U. S. Civil Service Commission announces an open competitive examination for the position of associate biochemist (syphilis research) at a salary of $3,200 a year for a vacancy in the Syphilis Research Center, Johns Hopkins Hospital, Baltimore. The work consists of investigative or research work in antibody chemistry, pollen chemistry, the chemistry of the arsphenamines or related problems. Candidates must have completed a four year college course with major study in chemistry or chemical engineering. In addition they must have had at least three years of experience or postgraduate training or a combination of these, at least one year, in active investigations of the biochemistry of proteins. Applications must be filed with the U. S. Civil Service Commission at Washington, D. C., before December 28. The closing date is December 31 for the states of Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington and Wyoming.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 13, 1937.

The Growth of Social Services

In an address to the Society of Arts, the chairman, Lord Amulree, said that year after year social legislation advanced and new means were devised for mitigating the hardships which would otherwise be felt by some members of the community. The aggregate public expenditure on education, housing, old age pensions, health insurance, unemployment insurance, unemployment assistance, public assistance or poor relief was annually about $1,500,000,000. In addition, $460,000,000 was collected by way of contributions from employers and employed persons. Unless some catastrophe occurred that would arrest all progress, social legislation was likely to increase. At present emphasis was being placed on physical fitness, and there was increased interest in the subject of nutrition. There was a source from which might spring numerous projects of social amelioration, such as the state subsidization of games and sports and possibly artificial cheapening of food. Concern about the birth rate might well give an impetus to the movement in favor of family allowances and the subsidizing of wages.

Some hoped that education would bring about such a standard of social behavior that all men would give their best without the stimulus of material reward or the fear of hardship. Even though that hope might be justified, it was doubtful whether such progress would keep pace with the rapid development of the social services. If not, we might be faced with serious economic and social difficulties. The problems of population might in the near future be not only quantitative. Vistas were opened which were not always pleasant. For example, there was the possibility of compulsory training, restriction of choice of employment and regimentation and control in other directions where at present we shrink from it. Would the benefit of the material advantages we desired to confer be outweighed by the price to be paid in the sacrifice of freedom?

Decrease in Blindness in Children

A bill to help the blind by reducing from 50 to 40 the age at which they become eligible for old age pensions was unanimously given a second reading in the House of Commons. The minister of health said that there were 78,000 registered blind persons in Great Britain. In consequence of increased knowledge of the causes of blindness which operated at birth or in early years and the preventive steps taken, the age at which blindness occurred was becoming later. There had been a substantial fall in the numbers of blind children. Those between the ages of 5 and 16 had fallen since 1925 from 3,104 to 1,916, a decrease of more than 38 per cent. It was not practicable to train a blind person after 40 for a new occupation. This was the reason for choosing that age in the bill. The only criticism made in the debate was that still more should be done for the blind. A medical member, Sir Francis Edward Fremantle, complained that no similar provision had been made for the deaf, whose case was almost as tragic as that of the blind. He also objected to extending a pension on a flat rate according to age and regardless of disability. The need of a blind person should be assessed and help given in a similar way to that followed in the case of ex-service men.

"A Relentless War on Rheumatic Disease"

In an address before the Empire Rheumatism Council, Lord Horder said that the problem of rheumatism had been gravely neglected from the aspect of scientific investigation and control. The reasons were not obscure. The rheumatic diseases were not dramatic, they were not directly lethal, and they were not specific in their causation. This very lack of a specific cause had been a potent factor in delaying thorough classification and research, a factor that was absent in such diseases as tuberculosis. It had been known for a long time that the causation of rheumatism was complex, and one after another a number of definite and important causative elements had been brought to light. We were now ready to advance systematically, both in the segregation of the different types of the disease and also in following the different indications for treatment. Since 1922, when the Ministry of Health began to reconnoiter the entrenched positions of the invading enemy, there had been increasing progress in organizing an effective attack on them. The Empire Rheumatism Council, formed last year, had already organized the scientific and administrative resources of the home country and the dominions for a relentless war on rheumatic disease.

The stresses and strains of modern life had greatly increased; more and more people were subjected to the bombardment of the din of the factory and of the city and to long periods of travel, often under conditions of overcrowding and jolting. The meals of thousands were hurried and defective in quantity or quality or both. A proper amount of physical exercise became more and more difficult for large masses of the people. Industry imposed on many a constant routine of small and frequently repeated movements which called for the overuse of a few muscles and the neglect of all the rest. These were the predisposing and, at times, even the determining causes of rheumatic diseases.

THE EXTENT OF THE SUFFERING

A Ministry of Health survey in 1922 showed that rheumatic disease was probably responsible for 16 per cent of the total industrial morbidity in this country and that during a year 372,600 insured persons sought medical advice for some form of rheumatic disease. The highest incidence was among metal workers, transport workers, mine workers, building workers and clerical workers, in that order. To that estimate of 372,600 insured persons had to be added those outside the insured class. They were considerable, but no basis existed for an accurate estimate. In the insured the annual monetary loss involved amounted to $85,000,000.

Rheumatism was not often directly lethal, but in rheumatic fever and in cardiac rheumatism there was a killing process second to none in the country. A Ministry of Health report for 1924 stated that "organic disease of the heart is for the most part rheumatic in origin and organic heart disease is the cause of over one third of all deaths."

A LONG TASK

The Empire Rheumatism Council proposed a plan of coordinated research into the causative factors and treatment of all the disease in the rheumatic group. Discovery of the causes would mean not merely cure but—what is more important—prevention. But the probability must be faced that the research might prove a long one. It was planned for a seven years term. All the existing treatments would be investigated simultaneously and any new ones brought to notice. Problems of infection, of biochemistry, of diet and of living and working conditions would be probed. The investigations would shortly cover the whole area of the British Empire, with its wide differences of climate and of habits. Also cooperation would be extended to all foreign effort. In therapeutic research, results could be hoped for in a short time. After arrival at the standardization of the most efficient and the most practicable treatment, the next step would be to make it available to all classes and to see that it was applied in the early stages. In a sentence, it was a ruthless war that was being planned, not against fellow men but against a savage enemy of the human race.

Sir Kinsley Wood, minister of health, has laid the foundation stone in London of an arthritis unit, the first of its kind in this country, which has been established by the Empire Rheumatism Council. He said that one sixth of our industrial invalidity was due to rheumatism. The unit marked a new step forward. It would provide beds for research in the early stages of the disease as well as prolonged investigation by a team of workers.

Research in Immunology

In the annual report of the London School of Hygiene and Tropical Medicine it is stated that an important advance has been made by joint researches in the departments of bacteriology and biochemistry. Chemical fractions which appear to have effective immunizing powers have been isolated from the organisms of typhoid, whooping cough and cholera and from certain strains of hemolytic streptococci. A point has been reached where practical application of the results obtained with some of these organisms is within view. The work appears to be of the utmost importance and likely to give a new direction to practice in relation to the whole group of infectious diseases.

PARIS

(From Our Regular Correspondent)

Nov. 6, 1937.

French Gynecologic and Obstetric Congress

The tenth Gynecologic and Obstetric Congress was held October 1-2 in Paris, the president being Professor Mocquot. The three subjects chosen for discussion were medical and surgical treatment of pruritus vulvae, uteroplacental apoplexy, and treatment of incontinence and of vesicovaginal fistula.

The first paper was by Vayssière of Marseilles on the etiology and treatment of pruritus vulvae. He said that from 8 to 10 per cent of all patients who applied for treatment at gynecologic dispensaries desired relief for this condition. Among the local causes, leukorrheal discharge was the most frequent. The pruritus was more marked during menstruation and pregnancy. Hormonal factors, such as estrogenic insufficiency, also must be searched for in the etiology. Local treatment of the cervicovaginal infection must be governed by the p_H of the secretions, with acetic or lactic acid if they are too alkaline and vice versa. A 1:2,000 solution of silver nitrate is efficacious. A Trichomonas infection is best treated by acetarsone. Radiotherapy is to be recommended for cases resisting all other treatment. If there is evidence of hormone insufficiency, relatively large doses, from 3,000 to 50,000 units a week, should be given, of estradiol benzoate in oil, subcutaneously. Cotte of Lyons pointed out that surgical treatment was a last resort after all nonoperative methods had been unsuccessful. Minor methods include local injections of a 1:400 solution of quinine and urea hydrochloride, of 60 to 90 per cent alcohol and of radioactive preparations. Presacral nerve resection had given good results in ten of seventeen cases; four were partly successful and three were failures. This operation is indicated only when every other method has failed to give relief. In the discussion, Labhardt of Switzerland stated that pruritus was a symptom in inflammatory disorders of the vulva, in psychoneuroses and in vulvar leukoplakia, owing as a rule to ovarian dysfunction. The leukoplakias responded to injections of estrogen, if relatively large doses were given. Kreis of Strasbourg emphasized the necessity of a search for psychoneuroses in the etiology. Jeanneney of Bordeaux said that the choice of neutralizing solutions and antiseptics to be employed depends on the results of the chemical and bacteriologic examination of the vaginal secretions. Search should be made for diabetes, hyperglycemia, high blood urea content and syphilis, next for evidences of ovarian dysfunction, and finally for disturbances of the sympathetic nervous system. Brocq and Dessaux of Paris reported a case successfully treated by vulvectomy after every other method had been tried.

The second subject for discussion was uteroplacental apoplexy. Professor Couvelaire pointed out that the subject included not only retroplacental hematoma and resultant hemorrhage but also bleeding into the uterine wall, perhaps extending to all the internal genitalia and other viscera. The pathogenesis is not clear. It was thought to be related to nephritis and hypertension in multiparas beyond the age of 30, but it has been found that it is not dependent on vascular lesions or hypertension. The former play a part during pregnancy and then only the capillaries are involved. Experimentally, these accidents appear to take place in women previously sensitized to various antigens, which makes them resemble the visceral infarcts by intolerance shock as described by Grégoire and Duval. The ovum does not take any part because the same phenomena can be produced in nonpregnant animals.

The treatment was the subject of a paper by Weymeersch and Snoeck of Belgium. The incidence of uteroplacental apoplexy varies from 0.09 to 1.06 per cent according to various reports. The obstetric methods of treatment aim to empty the uterus as rapidly as possible. Surgical intervention includes conservative cesarean section (high or low) alone or followed by vaginal hysterectomy and abdominal hysterectomy. Obstetric treatment was employed in 853 of 1,080 cases, with a maternal mortality of 6.58 per cent and a fetal mortality of 61.3 per cent. Surgical treatment in 227 cases entailed a maternal mortality of 21 per cent and a fetal mortality of 70.7 per cent.

The severity and extent of the hemorrhages are not necessarily a criterion of the gravity of the case in deciding which of the three operative methods is to be selected. The time factor is the most important one. If the uterus is emptied during the first ten hours after appearance of the symptoms, the maternal mortality is 27 per cent. It rises to 40 per cent if the ten hour period has been passed. Many obstetricians, in order to judge the functional value of the uterus, inject solution of posterior pituitary intravenously following cesarean section. If the uterus contracts well, so that no late hemorrhage is to be feared, the organ is conserved. Clinically the cases can be placed in two groups so far as treatment is concerned:

1. Hemorrhage preceded, accompanied or rapidly followed by the beginning of labor. In these, expectant treatment is the best. Morphine is given to relieve the pain, the bag of waters is ruptured, solution of posterior pituitary is given and eventually low forceps are used.

2. Severe hemorrhage appearing before any signs of labor and the general condition indicating a probable uteroplacental apoplexy. Some recommend expectant treatment with artificial rupture of the bag of waters. Others, in severe cases, with marked shock and a toxic syndrome, feel that only operative intervention can be considered, preferably low cesarean section.

In the discussion, Voron and Pigeaud of Lyons reported that, if the serum of patients suffering from purpura is injected into pregnant rabbits, visceral and intra-ovarian hemorrhages follow which resemble in every respect the lesions observed in uteroplacental hemorrhages in human beings. Brindeau and Lantuéjol of Paris reported two maternal and thirty-one fetal deaths in forty-three cases. Normal labor occurred in twenty-five but operative intervention was necessary in eighteen. Cathala of Paris believes that obstetric procedures (especially embryotomy) are preferable to surgical treatment. Conservative cesarean section is rarely indicated. Cesarean section with hysterectomy should be reserved for cases in which embryotomy is dangerous. De Snoo and Streink of the Netherlands are partisans of obstetric methods combined with the administration of remedies to combat the shock. In 214 cases there were only eleven maternal deaths (5 per cent) but a fetal mortality of 78 per cent. Le Lorier of Paris has been obliged to operate in only six of sixty-four cases, with two deaths (maternal). In two of the six a hysterectomy was necessary, with one death. Keller of Strasbourg was obliged to operate in only three of

twenty-seven cases. Eleven of eighteen women who were observed later became pregnant again and there were sixteen pregnancies with fourteen living children and no recurrence of a uteroplacental apoplexy. Ecalle and Suzor of Paris believe that a distinction should be made between premature detachment of a normally inserted placenta of toxic origin and uteroplacental apoplexy. In 14,000 obstetric cases they have observed the latter only seven times. All patients were operated on, with two deaths.

The first part of the third question for general discussion was the treatment of incontinence. The paper was read by Muret and Rapin of Switzerland. After a review of the anatomy of the female urethra, the authors stated that the most frequent cause is to be found in perineal and other lesions incident to parturition followed by incomplete postpartum involution. Next in order as causes are congenital or acquired relaxation of the tissues as well as the sequels of gynecologic procedures. As prophylactic measures, avoidance of prolonged labor, immediate repair of all lacerations and surveillance of uterine involution are to be recommended. Only surgical procedures offer any permanent relief. The various types of plastic operation were described and the conclusion was reached that an anterior colporrhaphy, which would include the sphincteric structures, would suffice in the majority of cases. A colpoperineorrhaphy should always be done at the same time.

The second part of the third question took up the treatment of vesicovaginal fistula and was presented by André of Nancy. As to etiology there were two groups: (*a*) fistulas incident to prolonged labor with pressure of the fetal head on the bladder or application of forceps and (*b*) operations on the uterus, especially total or radical hysterectomy and application of radium for cancer of the cervix. In the first group the fistulas are low, in the second much higher. Before any operation is planned, the relation of the fistula to the ureteral orifices must be ascertained by cystoscopic examination and the vagina should be dilated by tampons. The various types of operation were described, preference being given to the transvesical technic described by Marion, in fistulas following labor or operative procedures, when the opening is very high and the vagina narrow. The transperitoneal (Legueu) method is especially to be recommended, although difficult, in high lying fistulas following total hysterectomy. In the discussion, Vanverts of Lille said that immediate perineal repair required good light and technic. If these were not available, it would be preferable not to attempt a primary closure but do this later under proper conditions. Aubert of Switzerland and Hartmann of Paris maintained that the vaginal method sufficed for both low and high fistulas.

A paper was read by Claude Béclère of Paris on functional uterine hemorrhages. Hysterosalpingography permits differentiation of hemorrhages due to pathologic lesions (from 25 to 30 per cent of the cases) from those of functional origin (from 60 to 70 per cent of the cases). Among the latter, one can identify (*a*) functional hemorrhages in virgins, (*b*) those of congenital origin, (*c*) those due to ovarian infection in young women, and (*d*) premenopausal disturbances. All are characterized histologically by a benign hyperplasia of the uterine mucosa and radiologically by a dentated aspect of the uterine shadow. In *a* and *b* the administration of progestin gives excellent results and in *c* vaccinotherapy and diathermy are indicated, while in *d* roentgenotherapy is to be used.

French Otorhinolaryngologic Congress

This year's French Otorhinolaryngologic Congress was held October 17-20 at the Paris Medical School under the presidency of Professor Brémond of Marseilles. The evening before the opening of the congress, a meeting of the Society for Broncho-Esophagoscopy was held. The first subject chosen for special reports and general discussion for this year's congress of the parent society was "Indications and Results of Intracranial Surgery of the Auditory Nerve." The report had been prepared by Drs. Maurice Aubry and Marcel Ombrédanne of Paris. Full credit was given to the work of Dandy, who first showed the value of section of the auditory nerve in Ménière's disease. There is a direct etiologic relation between an adjacent arachnoiditis and an atypical Ménière syndrome. Section of the acoustic nerve presents no technical difficulties but there are certain contraindications, such as the age of the patient, hypertension, a developing otitic condition and an acute anterior meningitis. Of forty-six surgical cases, complete division was done in twenty-five and partial division in nineteen, while a tumor of the auditory nerve was removed in two. In the uncomplicated cases, all the operations were successful. Only patients with marked vertigo which has resisted all other forms of treatment should be operated on. There is a chance that this operation will facilitate a more accurate study of the etiology of vertigo and of vestibular physiology.

The second report was on acute inflammation of the hypolarynx in children and had been prepared by Drs. Le Mée, Bloch and Bouchet. Up to the present, this condition has been considered to belong to pediatrics rather than to laryngology, but there appears to be no contraindication to the use of endoscopic methods in both diagnosis and treatment. These severe forms of laryngitis have their origin in the subglottic portion of the larynx, termed "hypolarynx," and involve a very narrow portion in young children, among whom edema can easily occur because of the folds of the mucosa and the many lymphoid structures. This subglottic zone is hyperesthetic and easily gives rise to reflexes. These subglottic forms of laryngitis include a type in which spasm predominates; i. e., the stridulous form, an asphyxiating type with marked edema, a localized type with tendency to abscess formation, and an acute fulminant type of laryngitis accompanied by tracheobronchitis in which thick exudates or membranes form which can completely occlude the lumen of these structures. The last named condition has been studied more in the United States than elsewhere because of the more widespread use of broncho-esophagoscopy. The diagnosis can be made by this method, but the first problem that presents itself is to distinguish the endoscopic picture from that of a diphtheria or a reaction due to the presence of a foreign body. Low tracheotomy performed at an early period of the condition, as recommended by Chevalier Jackson, is preferable to intubation, because of the faulty construction of the cannula usually employed. Tracheotomy ought to be followed by aspiration and intrabronchial instillations. The importance of using moist heat and of various forms of apparatus in which oxygen or, better still, a nitrous oxide-oxygen or oxygen-helium mixture was used was emphasized. All children's hospitals should have trained endoscopists attached to their staff to meet such emergencies as acute inflammations of the hypolarynx present. They should also be equipped with the necessary apparatus for physical therapy.

Drs. Hicquet and Scherer of Brussels, in a paper on radiography of the larynx with the aid of opaque mediums, stated that profile views were the best. Dr. Worms called attention to osteosarcomas of the mastoid in young children, in which the earliest sign was an increase in size of the mastoid. Drs. Canuyt and Gunsett of Strasbourg stated that tomography, i. e., radiography in sections, was very useful in the early diagnosis of laryngeal cancer.

Eight personal observations of keratosis of the external auditory canal were reported by Rendu of Lyons. Curietherapy of endolaryngeal cancer by a special technic was the subject of a paper by Dr. Quanquin of Dijon. Drs. Le Mée and Bernard of Paris reported 41 per cent cures following the first six sittings in seventy-four cases of mastoiditis treated by mild doses of roentgen rays.

BERLIN

(From Our Regular Correspondent)

Oct. 25, 1937.

Developments in the Sickness Insurance

New regulations with regard to the admission of physicians to the sickness insurance practice have just been promulgated. For every 600 sick insurance club members a physician will be allowed to practice who has completed at least two years of preparatory service. Permits already granted under the older law are not affected by the new. In the selection from among candidates for the panel practice, preferment is given above all to physicians who have been active for at least two consecutive years at the public health headquarters of the Nazi party and to physicians who have been professionally active for at least one year in military or work service. On the other hand, doctors who served during the World War are no longer given preferment. Mere membership in the Nazi party is no longer a basis for preferment; a candidate must have a record of noteworthy services to the party. German physicians residing abroad who have rendered signal services to Germany or to German science are now as before admitted to the practice under special conditions. Physicians severely wounded in the World War are still accorded consideration. In addition a married candidate comes in for special consideration and the more children he has the greater the likelihood that he will be admitted. Other groups which receive preferment are doctors who have been in insurance practice in the country or in small cities for at least five years and who are seeking posts in the larger cities in order to provide their children with better educational advantages and doctors who have no assured income from property or pensions. No physician is admitted to panel practice if there exist serious personal grounds for rejection, such as addiction to drugs, political unreliability, married status of a woman physician whose family income from insurance practice would not be necessary to the economic security of the family, and simultaneous maintenance of a dental practice. As under the old regulations, any doctor is excluded from insurance who is married to a person of non-German or unrelated blood; namely, to one who would previously have been designated "non-Aryan." The national führer of the sickness insurance associations of Germany is empowered to make exceptions in cases which involve so-called hybrids, but each such case will be decided by this official on its individual merits. Presumably only hybrids of the second class would be considered; namely, persons in whose ascendency there is but one pair of Jewish grandparents.

It is a well known fact that under the old regulations an important principle had come to be accepted (especially since the standardization of sickness insurance in Germany); namely, that the insurance patient like any private patient was permitted (with certain limits) a free choice of physician. Although not all private practitioners were accustomed to treat insurance patients, the roster of the insurance physicians was formidable and accordingly a patient encountered little to prevent his "freedom of choice." But this situation has been changed. At the party congress in Nuremberg the national führer of physicians, Dr. Wagner, delineated contemplated restrictive measures on the patient's free choice of a physician. The following is a paraphrase of Wagner's remarks: A change will take place in the immediate future. In order to strengthen the bonds between the family physician and his patients, the insured person must now elect the services of a particular doctor for the period of one year and can consult no other during this time, either for his own illness or for that of the members of his family. Thus is inaugurated a new policy of supervision that affects both the physician and the insured. The insurance doctor has till now received compensation only according to the number of patients treated and this meant that he had a definite economic interest in the number of sick certificates issued by him. The new legislation introduces a radically different system: the insurance doctor will be paid a certain sum for the care of the insured and the insured's family, an arrangement formerly sometimes applied to family doctors. Consequently the insurance doctor no longer has an economic stake in the number of sickness certificates or the amount of illness but, conversely, it is to his advantage that his patients remain in health, as illness now means only additional work for him without extra compensation.

The foregoing statement of the national führer of physicians is in many respects revealing. His comparison of the new system with that formerly in vogue among family physicians is not exactly fair, since the annual honorarium of the insurance doctor, as envisaged in the new law, must naturally be much smaller than that formerly received by the family practitioner. Of much greater significance is the psychologic aspect of the change, for whereas previously physician and patient could quickly conclude any agreement without the interference of a third party, the ubiquitous Institute of Social Insurance now enters into a sort of partnership with the patients and this anonymous "partner" constantly makes its presence felt. This is the "supervision" mentioned by Dr. Wagner and which, although needed for purposes of administration, is capable of exercising a definite influence on the relationship (or on the psychologic relationship, at least) between doctor and patient. Yet even more important than this and the essential feature of the new policy is the argument with regard to the striking reversal of the physician's material interest; namely, that the doctor will now benefit from the continued health of his patients rather than from their illnesses. Apart from many exaggerations which certainly (consciously or as in most instances unconsciously) had been present, the insurance doctor had become, so to speak, the "advocate" of his patients in their claims against the insurance clubs for any kind of special treatment or medicament. But does not the possibility exist under the new plan, with its mentioned displacement of economic interest, that a doctor motivated by the wish to see naught but health may relax his careful observation of insurance patients or, quite unconsciously, become loath to recognize true disease? This possible development has been cautiously urged by other critics of the new plan, but the führer of physicians appears to consider it of less importance than the opposite tendency, which, as he mentioned in his speech, leads the doctor to look everywhere for disease. This problem is thus by no means solved and one can only await a further turn of events.

The organization of the sick insurance has been simplified by a new ordinance that became effective October 1. Henceforth there will be four national associations of sickness insurance clubs: municipal, rural, industrial and guild. All are under the jurisdiction of the national minister of labor. Every sick insurance club must be affiliated with one or another of these national associations. The latter serve the individual clubs in an advisory capacity in matters pertaining to the termination or alteration of contracts with the organized representatives of the medical profession, institutions for the sick, dealers in supplies used by the sick insurance and so on. Furthermore, among other administrative functions the national associations supervise the prompt settlement of all honorariums paid out by the member clubs to the physicians. In future, the four national associations will be the only organizations of affiliated insurance clubs; other such organizations (about 100 of which were still in existence October 1) have been dissolved. The new law also provides that no insurance association can any longer represent one-sided interests, as occasionally happened under the old organization.

As reported previously, a comprehensive nationalization of independent insurance clubs has been in progress for quite

some time. In the past, many of these independent clubs ran into financial difficulties and not the least reason for this was their small size, which prevented them from maintaining the necessary actuarial balance. As a rule this situation led to increased expenditures that exceeded the income from contributions. The reforms in organization of the sickness insurance, which went into effect in 1933, were chiefly aimed at the creation of larger spheres of activity for weakly functioning and financially embarrassed clubs by consolidation of these clubs with other more solvent clubs. As a result of this program the number of independent clubs declined by around 2,000 during the years from 1933 to 1937; namely, from about 6,550 to 4,600. Most pronounced were the declines in the number of municipal clubs (from about 2,000 to 900) and the guild clubs (from about 800 to 300). As a further result of this reorganization the average premium rate in the municipal clubs dropped from 5.7 per cent in 1933 to 5.4 per cent in 1933; in the guild clubs there was a corresponding decline from 4.9 per cent to 4.7 per cent during the same period. These reductions were effected without any curtailment of benefits to members. On the contrary, the services of the clubs were able to function more adequately because of the sounder financial position.

The German Substitute for the Nobel Prize

A law was recently passed in Germany, motivated by political consideration and specifically by dissatisfaction with the selection of a Nobel peace prize winner, according to which German citizens are no longer permitted to accept a Nobel prize, and a national prize was created as a substitute (THE JOURNAL, April 17, 1937, p. 1354). This new prize has just now been awarded on the occasion of the party congress in Nuremberg. Two physicians were among the prize winners: Professor Sauerbruch, Berlin ordinarius in surgery, and Professor Bier, the surgeon, now retired. The cash prize was divided between the two men so honored, each of whom received 50,000 marks.

BUENOS AIRES

(From Our Regular Correspondent)

Oct. 20, 1937.

Experimental Hypertension

Profs. B. A. Houssay and J. C. Fasciolo, in lectures delivered at the Academia Nacional de Medicina and the Sociedad Argentina de Biología, reported studies on experimental arterial hypertension induced by compressing the renal artery according to the technics of Goldblatt, Lyneh and Summerville. In arterial hypertension induced by unilateral compression of the renal artery, removal of the ischemic kidney results in normalization of the blood pressure, which continues normal after the experiment. Implantation of the ischemic kidney and its compressed renal artery, by uniting the renal artery to the carotid artery and the renal vein to the jugular vein in the neck of a dog in hypertension which was recently nephrectomized and treated with chloralose, increases the arterial pressure of the receptive dog, within five or ten minutes, 40 or 70 mm. of mercury up to an approximate high level of 200 mm. of mercury. If the grafted kidney is removed, hypertension does not diminish but continues high for the first two or three hours after its removal. If the kidney is transplanted in another dog in the same condition as the former, the same increase of arterial pressure is induced in the former as in the latter. The blood pressure of receptive dogs does not increase if the transplanted kidney is normal, whether the structure was removed from a normal dog or from a dog in a state of hypertension. Transplantation of both normal kidneys induced intense hypertension only in two dogs and slight hypertension in one. The experiments prove that the ischemic kidney secretes substances that cause permanent arterial hypertension.

New Teaching Chairs

The Escuela de Medicina of Buenos Aires recently had thirty-eight teaching chairs, and lately chairs have been established for the teaching of semeiology, nutritional diseases, neurosurgery, history of medicine and puericulture. Profs. R. Izzo, Pedro Escudero, M. Balado, J. P. Beltrán and Pedro de Elizalde are the appointed teachers. Four physicians were appointed assistant professors to the classes of surgical pathology. The Escuela de Odontologia of Buenos Aires increased the teaching chairs from six to sixteen. Discussions are made on the subject because of the fact that there are neither rooms nor money enough for incurring new expenses. The money allowed for teaching expenses has been cut down, since 1930, to almost half the original amount.

Fellowships

Fellowships have been granted as follows: From the Asociacion Argentina para el Progreso de las Ciencias to Drs. Moisset de Espanés, A. Manso Soto, Schwarz and Pirosky. They will do special studies on pharmacology and bacteriology in Paris, London and the Pasteur Institute of Paris, respectively.

The Academia Nacional de Medicina granted the Devoto fellowship to Dr. N. G. Foglia, who will work first with Professor Collip of the McGill University in Montreal and then in the United States.

The Comisión Nacional de Cultura granted a fellowship to Dr. Introzzi to study surgery in hypertension and to Dr. J. C. Nuñez to study gastro-enterology in the United States.

The Rockefeller Foundation granted a fellowship to C. M. Pomerat of Clark University to work in the Instituto de Fisiología of the Faculty of Medicine of Buenos Aires.

Drs. N. Ludueñz, J. B. Odoriz and C. A. Tanturi came back home after having made fellowship studies. Dr. Ludueña worked on pharmacology at Oxford, Dr. Odoriz worked on neurophysiology at Oxford and the Rockefeller Institute in New York and Dr. Tanturi worked in the Department of Physiology of the Northwestern University Medical School in Chicago.

Deaths

Dr. Manuel A. Santas, substitute ex-professor of pediatrics of the Faculty of Medicine of Buenos Aires and adviser to the faculty, is dead.

Dr. Miguel Angel Finochietto, head of the ward of practical work in descriptive anatomy of the Faculty of Medicine of Buenos Aires, is dead.

Dr. Ricardo Colon, a fellow of a number of the Academia Nacional de Medicina, died recently at the age of 77.

Marriages

ADLAI STEPHENSON LILLY, Richmond, Va., to Mrs. Sarah Bugg Gholson of Henderson, N. C., October 23.

POTTER A. RICHARDS, Vinton, Va., to Miss Margaret Frances Morrison of Rockbridge County, September 18.

LEO BROWN SKEEN to Miss Frances Elizabeth Ashburn, both of Troy, N. C., in Durham, September 13.

THOMAS ADDISON MORGAN, Franklin, Va., to Miss Margaret Virginia Ellis., in Ashland, September 4.

ARAL C. SORENSON, Davenport, Iowa, to Miss Margaret Bagley of Chicago, October 16.

LOUIS C. POSEY to Miss Mamie Lowe Walker, both of Birmingham, Ala., October 2.

LEVIN HENDERSON PEEK to Miss Frances E. Osborn, both of Cherokee, Iowa, October 8.

CHARLES K. PADGETT to Mrs. Virginia Hoey Smith, both of Shelby, N. C., November 2.

RAYMOND V. MCCRAY to Miss Martha Brown, both of Malvern, Ark., October 15.

HOMER R. MAULDING, Atlanta, to Miss Thelma Irene Ivey, September 26.

Deaths

William Craig Meanor ✠ Pittsburgh; University of Pennsylvania Department of Medicine, Philadelphia, 1895; member of the American Academy of Ophthalmology and Oto-Laryngology; fellow of the American College of Surgeons; served during the World War; surgeon, Beaver Valley General Hospital, New Brighton, Rochester General Hospital, Rochester, Pa., and the Valley Hospital, Sewickley; aged 65; died, September 25, of cerebral hemorrhage.

Sinclair Tousey, Garden City, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1888; surgeon, outpatient department, Roosevelt Hospital, New York, 1891-1900; formerly director and consulting surgeon of the St. Bartholomew Clinic and Hospital; author of "Medical Electricity and Röntgen Rays"; aged 73; died, September 25, in the Morrison Hospital, Whitefield, N. H., of valvular heart disease.

Solomon Jones ✠ Danville, Ill.; Illinois Medical College, Chicago, 1902; past president and secretary of the Vermilion County Medical Society; past president of the Aesculapian Medical Society of the Wabash Valley; fellow of the American College of Surgeons; formerly member of the city board of education; on the staff of the Lake View Hospital; aged 65; died, September 25, of cerebral hemorrhage.

John Crego Lester ✠ New York; Long Island College Hospital, Brooklyn, 1879; member of the American Otological Society; fellow of the American College of Surgeons; assistant surgeon, New York Eye and Ear Infirmary; aged 81; died, September 25, in the House of Mercy Hospital, Pittsfield, Mass., of diabetes mellitus, hypostatic pneumonia and hypertrophy of the prostate.

Warren Wilson ✠ Northfield, Minn.; Chicago Medical College, 1889; an Affiliate Fellow of the American Medical Association; past president of the Rice County Medical Society; served during the World War; for many years member and secretary of the school board; on the staff of the Northfield City Hospital; aged 74; died, September 4, of heart disease.

Henry Martin Cass, Johnson City, Tenn.; Vanderbilt University School of Medicine, Nashville, 1900; member of the Tennessee State Medical Association; fellow of the American College of Surgeons; veteran of the Spanish-American and World wars; on the staff of the Appalachian Hospital; aged 62; died, September 13, of coronary thrombosis.

Thomas Jefferson Brothers ✠ Anniston, Ala.; College of Physicians and Surgeons, Baltimore, 1903; fellow of the American College of Surgeons; past president of the Calhoun County Medical Society; served during the World War; surgeon to the Garner Hospital; aged 57; died, September 1, of coronary thrombosis and arteriosclerosis.

William Grosvenor Fulton, Scranton, Pa.; Bellevue Hospital Medical College, New York, 1886; fellow of the American College of Surgeons; consulting surgeon, Scranton State and Moses Taylor hospitals, Scranton, Nesbitt Memorial Hospital, Kingston and Carbondale (Pa.) General Hospital; aged 76; died, September 27, of arteriosclerosis.

George W. Allaman ✠ Atchison, Kan.; Ensworth Medical College, St. Joseph, Mo., 1892; past president of the Atchison County Medical Society; formerly member of the state legislature, member of the city council and mayor of Atchison; on the staff of the Atchison Hospital; aged 74; died, September 24, of cerebral hemorrhage.

Frederick Ellis Jones, Quincy, Mass.; Harvard University Medical School, Boston, 1897; member of the Massachusetts Medical Society; served during the World War; formerly health officer; aged 64; on the staff of the Quincy City Hospital, where he died, September 29, of chronic interstitial nephritis and mesenteric thrombosis.

Peter Drummond, Grant, Mich.; Trinity Medical College, Toronto, Ont., Canada, 1888; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1889; member of the Michigan State Medical Society; formerly village president and president of the school board; aged 70; died, September 24, of coronary thrombosis.

Clarence Augustus Shimansky, Sandusky, Ohio; University of Michigan Homeopathic Medical School, Ann Arbor, 1898; member of the Ohio State Medical Association; aged 62; on the staffs of the Providence Hospital and the Good Samaritan Hospital, where he died, September 13, of intestinal obstruction.

Leroy Taylor Howard ✠ Lieutenant Colonel, U. S. Army, Hyattsville, Md.; Georgetown University School of Medicine, Washington, D. C., 1913; served during the World War; entered the medical corps of the U. S. Army as a first lieutenant in 1917; aged 48; died, September 30, of arteriosclerosis.

Thomas William Smith, Newberry, S. C.; Louisville (Ky.) Medical College, 1891; member of the South Carolina Medical Association; past president of the Newberry County Medical Society; chairman of the board of health of Newberry; aged 68; died, September 11, in a hospital at Columbia.

Frank Alembert Brayton, Indianapolis; Indiana University School of Medicine, Indianapolis, 1912; served during the World War; associate in dermatology and syphilology at his alma mater; on the staffs of the City and Methodist hospitals; aged 47; died, September 20, of heart disease.

Jules Louis Prevost, Port Providence, Pa.; Temple University School of Medicine, Philadelphia, 1909; also a clergyman; formerly lecturer on history of medicine and medical terminology, at his alma mater; at one time a missionary in Alaska; aged 74; died, September 2.

John Lee, Detroit; Detroit College of Medicine, 1890; formerly assistant professor of medicine at his alma mater; veteran of the Spanish-American War; for many years on the staff of St. Mary's Hospital; aged 68; died, September 22, of chronic nephritis and myocarditis.

Charles William Huff, Jackson, Wyo.; Baltimore Medical College, 1912; member of the Wyoming State Medical Society; fellow of the American College of Surgeons; on the staff of St. John's Hospital; aged 49; died, September 22, at Idaho Falls, Idaho, of agranulocytosis.

Thomas Henry Hall, Brighton, Ill.; Rush Medical College, Chicago, 1884; member of the Illinois State Medical Society; formerly mayor, and member of the board of health; aged 77; died, September 10, of sarcoma of the pelvic bones with metastasis to lungs and other organs.

George R. Clayton, Monon, Ind.; Kentucky School of Medicine, Louisville, 1880; member of the Indiana State Medical Association; for many years member of the school board; health officer; aged 83; died, September 8, at Rensselaer, of carcinoma of the rectum.

Pedro G. Acosta, Rome, N. Y.; University of Santo Tomas College of Medicine and Surgery, Manila, P. I., 1925; for several years resident physician to the Oneida County Hospital; aged 36; died, September 28, of chronic interstitial nephritis and cerebral hemorrhage.

Marion Blaisdell MacMillan, Milwaukee; University of Texas School of Medicine, Galveston, 1898; formerly connected with the U. S. Veterans Bureau; aged 61; died, September 1, in the Epworth Hospital, South Bend, Ind., of perforated gastric ulcer and peritonitis.

William Robert Perdue, West Chester, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1874; member of the Medical Society of the State of Pennsylvania; aged 88; died, September 13, in the Chester County Hospital of chronic myocarditis.

Joseph Cameron McClurkin, Evansville, Ind.; Bellevue Hospital Medical College, New York, 1880; member of the Indiana State Medical Association; for many years on the staff of St. Mary's Hospital; aged 84; died, September 18, of cerebral hemorrhage.

Arthur Charles Wheeler, Erie, Pa.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1893; member of the Medical Society of the State of Pennsylvania; aged 68; died, September 4, in Waterford, of paralysis agitans.

Alice Catherine Fitzsimmons Lankford, Princess Anne, Md.; Woman's Medical College of Pennsylvania, Philadelphia, 1904; member of the Medical and Chirurgical Faculty of Maryland; aged 54; was found dead, September 28, of a self-inflicted bullet wound.

Ralph Allison Goodner, Anna, Ill.; Rush Medical College, Chicago, 1888; Jefferson Medical College of Philadelphia, 1891; medical superintendent and managing officer of the Anna State Hospital; aged 72; died, September 19, of enteritis and chronic myocarditis.

Leo Wesley Chilton, Boise, Idaho; University of Minnesota College of Medicine and Surgery, Minneapolis, 1904; served during the World War; for many years associated with the Veterans Administration Facility; aged 59; died, September 14.

George E. Webster, Kingsville, Ohio; Western Reserve University Medical Department, Cleveland, 1880; at one time coroner of Ashtabula County; aged 79; died, August 22, in the Deaconess Hospital, Cleveland, of hypertrophy of the prostate.

Milton H. Herbein, Macungie, Pa.; Jefferson Medical College of Philadelphia, 1879; member of the Medical Society of the State of Pennsylvania; aged 80; died, September 17, of cerebral thrombosis, arteriosclerosis, chronic myocarditis and nephritis.

James Samuel Hess, Mauston, Wis.; Barnes Medical College, St. Louis, 1893; member of the State Medical Society of Wisconsin; on the staff of the Mauston Hospital; aged 73; died, September 15, of chronic myocarditis and coronary occlusion.

Ord Otterbein Le Master, Sidney, Ohio; Starling Medical College, Columbus, 1902; member of the Ohio State Medical Association; aged 61; on the staff of the Wilson Memorial Hospital, where he died, September 15, of an impacted gallstone.

Albert Samuel Wall, Los Angeles; Miami Medical College, Cincinnati, 1890; member of the California Medical Association; past president of the Champaign County (Ill.) Medical Society; aged 76; died, September 9, of diabetes mellitus.

Leopold Kaffie, Corpus Christi, Texas; Louisville (Ky.) Medical College, 1903; member of the State Medical Association of Texas; aged 57; died, September 28, in a hospital at San Antonio, of myocarditis and carcinoma of the bladder.

William Pierce Fitzgerald, Gerald, Mo.; Missouri Medical College, St. Louis, 1887; member of the Missouri State Medical Association; aged 76; died, September 14, of injuries received in an automobile accident and hypostatic pneumonia.

David Beaty Frontis, Ridge Spring, S. C.; University of Maryland School of Medicine, Baltimore, 1880; member of the South Carolina Medical Association; aged 81; died, September 24, in the Columbia (S. C.) hospital, of pneumonia.

William E. Stemen, Grosse Pointe Park, Mich.; Fort Wayne (Ind.) College of Medicine, 1894; served during the Spanish-American and World wars; aged 67; died, September 12, of aortitis and chronic myocarditis.

Charles L. Willian, Buffalo, Ky.; Kentucky School of Medicine, Louisville, 1889; aged 76; died, September 25, in the Kentucky Baptist Hospital, Louisville, of arteriosclerosis, heart disease and hypertrophy of the prostate.

Edward Charles Kauffman ⊕ Union, Iowa; State University of Iowa College of Homeopathic Medicine, Iowa City, 1901; aged 65; died, September 16, in the Deaconess Hospital, Marshalltown, of coronary thrombosis.

Joseph Briggs Murphy, Taunton, Mass.; Harvard University Medical School, Boston, 1883; member of the Massachusetts Medical Society; aged 77; died, September 5, at Falmouth Heights, of heart disease.

David Gilbert Estes, Athens, Ala.; University of Tennessee Medical Department, Nashville, 1901; member of the Medical Association of the State of Alabama; aged 58; died, September 18, of coronary occlusion.

Jean Baptiste Archambault, Woonsocket, R. I.; School of Medicine and Surgery of Montreal, Faculty of Medicine of the University of Laval at Montreal, 1894; aged 69; died, September 21, of cerebral hemorrhage.

John Milton Smith, New Philadelphia, Ohio; Cincinnati College of Medicine and Surgery, 1880; for many years a member of the board of education; aged 81; died, September 5, of arteriosclerosis and uremia.

Don H. Hinckley, Chicago; Jenner Medical College, Chicago, 1909; aged 59; died, September 5, in the Victory Memorial Hospital, Waukegan, Ill., of injuries received in a fall from a tree.

Walter Q. Harper, Los Angeles; Kentucky School of Medicine, Louisville, 1898; on the staff of the Physicians and Surgeons Hospital, Glendale; aged 64; died, September 19, of coronary embolus.

Ulric Zwingle Junkermann, Pomeroy, Ohio; Cleveland-Pulte Medical College, 1913; served during the World War; aged 51; died, September 24, at his home in Middleport, of angina pectoris.

Isaac Chase Irish ⊕ Bowdoinham, Maine; Medical School of Maine, Portland, 1878; formerly member of the school board and health officer; aged 83; died, September 27, of carcinoma of the pancreas.

Joseph French Alsop, Prospect, Va.; University of Virginia Department of Medicine, Charlottesville, 1898; member of the Medical Society of Virginia; aged 68; died suddenly, September 4.

Flora Allison Wright, Tucson, Ariz.; University of Oklahoma School of Medicine, Oklahoma City, 1925; aged 42; died, September 9, in the Southern Methodist Hospital, of pulmonary tuberculosis.

Andrew John Heimark ⊕ Fargo, N. D.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; aged 57; died, September 17, of myocarditis.

Clarence Garrabrant, Atlantic City, N. J.; College of Physicians and Surgeons, Baltimore, 1886; aged 81; died, September 30, in a local hospital of chronic prostatitis with obstruction.

John Sidney Hood, Gastonia, N. C.; Jefferson Medical College of Philadelphia, 1907; member of the Medical Society of the State of North Carolina; aged 53; died suddenly, September 14.

Cooley S. Ellis, Lonoke, Ark.; Louisville (Ky.) Medical College, 1905; member of the Arkansas Medical Society; aged 61; died, September 4, of carcinoma of the stomach and chronic nephritis.

Henry A. McIlmoyl ⊕ Ogdensburg, N. Y.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1876; aged 83; died, September 21, of chronic endocarditis and acute parotitis.

Charles Hammond, Topeka, Kan.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1897; aged 63; died, September 17, of septicemia and endocarditis.

Leinster Duffy, New Bern, N. C.; College of Physicians and Surgeons, Baltimore, 1889; aged 79; died, September 29, of cirrhosis of the liver with biliary obstruction.

Edwin S. Lothrop, Washington, D. C.; Howard University College of Medicine, Washington, 1893; aged 67; died, September 23, of mediastinal tumor and carcinoma.

Frederick Stork ⊕ Wickliffe, Ohio; Cleveland Homeopathic Medical College, 1903; aged 73; died, September 12, of coronary thrombosis and lymphatic leukemia.

Anti Costa Watts, Birmingham, Ala.; Louisville (Ky.) Medical College, 1892; aged 67; died, September 12, at his home in Lewisburg, of chronic myocarditis.

Charles Joseph Roberts, Berwyn, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1882; aged 80; died, September 3, of myocarditis.

Oscar D. Whalin, Chicago; Rush Medical College, Chicago, 1890; aged 71; died suddenly, September 12, of cerebral hemorrhage and arteriosclerosis.

William Garr Shadrach, Culpeper, Va.; University of Virginia Department of Medicine, Charlottesville, 1892; aged 67; died, August 12, of cerebral hemorrhage.

Harry M. Lincoln, Wilton, N. Y.; Albany (N. Y.) Medical College, 1886; aged 79; died, September 24, of carcinoma of the gallbladder with metastasis to the liver.

Duff M. Hodges, East Prairie, Mo.; University of Tennessee Medical Department, Nashville, 1890; aged 81; died, September 20, of cerebral hemorrhage.

Solomon Oliver Mayerson, Chicago; Loyola University School of Medicine, Chicago, 1921; aged 48; died, September 2, of cerebral vascular hemorrhage.

Taylor Jirardeau Frierson, Augusta, Ga.; Leonard Medical School, Raleigh, N. C., 1902; aged 62; died, September 15, of heart disease and influenza.

John Washington Meek, Chicago; Rush Medical College, Chicago, 1881; aged 78; was found dead, September 17, of gunshot wounds of the head.

Erly H. Madison ⊕ Olean, N. Y.; University of Buffalo School of Medicine, 1891; aged 69; died, September 15, of heart disease and arteriosclerosis.

John R. Archer, North Baltimore, Ohio; Starling Medical College, Columbus, 1887; aged 77; died, September 4, of carcinoma of the stomach.

William Holmes Bryan, Pavo, Ga.; Atlanta Medical College, 1893; aged 69; died, September 1, of chronic nephritis and arteriosclerosis.

George F. Henry, Kelat, Ky.; Cincinnati College of Medicine and Surgery, 1879; aged 83; died, September 3, of valvular heart disease.

William B. McIntosh, Colfax, Ill.; Barnes Medical College, St. Louis, 1895; aged 71; died, September 8, of carcinoma of the prostate.

Edwin W. Duncan, Burlington, Ky.; Medical College of Ohio, Cincinnati, 1885; aged 76; died, September 28, of myocarditis.

Thomas S. McCoy, Bradenton, Fla.; Hospital Medical College, Atlanta, Ga., 1910; aged 58; died, September 27, of malaria.

Bureau of Investigation

MISBRANDED "PATENT MEDICINES"

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the United States Department of Agriculture

[EDITORIAL NOTE: The abstracts that follow are given in the briefest possible form: (1) the name of the product; (2) the name of the manufacturer, shipper or consigner; (3) the composition; (4) the type of nostrum; (5) the reason for the charge of misbranding, and (6) the date of issuance of the Notice of Judgment—which may be considerably later than the date of the seizure of the product.]

Tru Tablets of Asperin.—Blackstone Mfg. Co., Newark, N. J. Composition: 4.97 grains of aspirin per tablet. For acute rheumatism, gout, sciatica, tonsillitis, influenza, etc. Fraudulent therapeutic claims.—[*N. J. 25150; August 1936.*]

Bron-Ki.—Bron-Ki-Co., Columbus, Ohio. Composition: Eucalyptol and terebinthine. Fraudulently represented as a cure for bronchitis and kindred disorders.—[*N. J. 25381; October 1936.*]

Tipona Tablets.—Hi-Test Laboratories, doing business as Maison Laboratories, and Tipona Co., Cleveland. Composition: Essentially phenolphthalein (1 grain per tablet), caffeine, and desiccated thyroid (about ¼ grain per tablet). Fraudulently represented to prevent or eliminate fat, to produce muscle, bone and sound flesh, correct glandular disorders, resist disease germs, etc. The claim "No drugs of Any Kind" was also fraudulent.—[*N. J. 25385; October 1936.*]

Nurse Brand Blood Purifier.—DePree Co., Holland, Mich. Composition: Essentially potassium iodide and extracts of plant drugs including a laxative, with alcohol, sugar and water. On the label the plant drugs were declared to be Honduras sarsaparilla, dandelion root, burdock root and clover tops. Fraudulent therapeutic claims.—[*N. J. 25387; October 1936.*]

Sanacaps.—Jessie Rogers, trading as Osan Products Co., Chicago. Composition: Baking soda, tartaric acid, and a small amount of chloramine-T. Fraudulently represented as a germicide and a cure for leukorrhea and inflammation.—[*N. J. 25394; October 1936.*]

Rogers' (Dr.) Relief Compound.—Jessie Rogers, trading as Osan Products Co., Chicago. Composition: Aloe, a turpentine oil resembling oil of savin, and iron sulfate, coated with sugar and calcium carbonate. Fraudulently represented as a remedy for female disorders.—[*N. J. 25394; October 1936.*]

Obegyne (Formerly Medogyn Hygienic Vaginal Jelly).—Dayton Laboratories, Inc., Dayton, Ohio. Composition: Essentially water, glycerin, gum tragacanth, lactic acid, a quinine compound, hydroxyquinoline, and small amounts of resorcinol and zinc compound. Fraudulently represented as a cure for leukorrhea, vaginitis, and gonorrhea, as a prophylactic for gonorrhea and syphilis, and a germicide. Fraudulent therapeutic claims.—[*N. J. 25402; October 1936.*]

Grabill's (Dr.) Prescription No. 1313.—Hi-Test Laboratories, doing business as the Maison Laboratories, Cleveland. Composition: Tablets containing 7.71 grains of cinchophen each. For rheumatism, neuritis, arthritis, uric acid, etc. Fraudulent therapeutic claims.—[*N. J. 25405; October 1936.*]

BP Prescription.—DePree Co., Holland, Mich. Composition: Essentially potassium iodide, extracts of plant drugs including a laxative, with alcohol, sugar and water. For impure blood. Fraudulent therapeutic claims.—[*N. J. 25406; October 1936.*]

Lur-Eye Lash Developer.—Lur-Eye Products, Inc., New York. Composition: Essentially 1.3 per cent of volatile oils, including wintergreen and thymol, in a base of white petrolatum. For developing eyelashes, relieving bloodshot or inflamed eyes, and granulated lids. Fraudulent therapeutic claims.—[*N. J. 25409; October 1936.*]

Blackstone's Tru Laxative Bromides Quinine Cold Tablets.—Blackstone Mfg. Co., Newark, N. J. Composition: Essentially acetanilid (1.4 grains per tablet), quinine dihydrobromide (0.96 grain per tablet), and aloes. For la grippe, colds, coughs, etc. Fraudulent therapeutic claims.—[*N. J. 25413; October 1936.*]

Tru-Lax.—Blackstone Mfg. Co., Newark, N. J. Composition: Essentially phenolphthalein (1.7 grains per tablet) and chocolate, which was worm-eaten and contained wormy excreta. For sour stomach, jaundice, bad breath, headache, etc. Fraudulent therapeutic claims.—[*N. J. 25414; October 1936.*]

Lubrol.—Atlas Laboratories, Akron, Ohio. Composition: Water, boric acid (1.19 per cent), Irish moss, glycerin, starch, lactic acid, and a small amount of oxyquinoline sulfate. Fraudulently represented as a germicide and a remedy for leukorrhea, cervicitis, vaginitis, etc.—[*N. J. 25415; October 1936.*]

Knifers Tonic (Formerly Dr. Neuffer's Lung Tonic).—McMurray Drug Co., Abbeville, S. C. Composition: Essentially creosote, a chloride, alcohol (37 per cent), and water. For coughs, bronchial asthma, etc. Fraudulent therapeutic claims.—[*N. J. 25420; October 1936.*]

Pneumo-Nox.—Willard Products Co., Greenville, N. C. Composition: Essentially volatile oils, including menthol and eucalyptol, in petrolatum. For bronchial and lung troubles. Fraudulent therapeutic claims.—[*N. J. 25421; October 1936.*]

Wittone.—United Distributors, Inc., Louisville, Ky. Composition: Essentially epsom salt, salicylic acid and water, flavored with cinnamon. Fraudulently represented as a cure for headache, chronic malaria, rheumatism, impure blood, etc.—[*N. J. 25423; October 1936.*]

Krispy Krumbs.—Better Wheat Foods Co., and Denton Rogers, Logan Utah. Composition: Essentially wheat containing a large amount of bran, with little, if any, flaxseed present. Misbranded in the statement "100% Whole Wheat," whereas it was not. Fraudulently represented as a remedy for stomach ulcers, kidney and liver disorders, rheumatism, diabetes, etc.—[*N. J. 25851; January 1937.*]

Exserco Antiseptic Deodorant Disinfectant.—Exterminating Service Co., Inc., Pittsburgh. Composition: Essentially soap, water, coal-tar neutral oils, and phenols. Fraudulently represented as an antiseptic and disinfectant, and an effective treatment for hair and scalp, a douche, and a remedy for chapping, itching and minor wounds.—[*N. J. 25805; January 1937.*]

Gyptol.—Folsom Extract Co., Inc., Lynn, Mass. Composition: Soap, phenols, coal-tar neutral oils, and water. Fraudulently represented as an antiseptic if used according to directions, and a pain remedy.—[*N. J. 25806; January 1937.*]

Sanderson's (Dr. P. C.) Indian Herbs of Joy and Blood Cleanser.—Aschenbach & Miller, Inc., Philadelphia. Composition: Ground crude drugs including aloe, cinnamon and ginger. Fraudulently represented as a blood cleanser, health promoter, and a treatment for liver disorders, dyspepsia, rheumatism, malarial fevers, etc.—[*N. J. 25819; January 1937.*]

Sulfo-Kresol-Tabs.—Ehrhart & Karl, Inc., Chicago. Composition: Oxyquinoline sulfate (slightly more than ¼ grain per tablet) and milk sugar; free sulfur and creosol were not found. Misbranded because of misleading name; fraudulently represented as a cure for inflammatory conditions, septicemia and ulcerated throat.—[*N. J. 25802; January 1937.*]

Calumet Herb Tea.—Joseph E. Meyer, trading as Indiana Botanic Gardens, Hammond, Ind. Composition: Dried plant material including senna leaves, juniper root, cascara bark, fennel seed, licorice, mallow root, leaves, flowers and unidentified woody material. Fraudulently represented as a remedy for aching joints, nervousness, all disorders due to constipation, including cancer, etc.—[*N. J. 25812; January 1937.*]

Kloria.—Kloria Co., Fort Wayne, Ind. Composition: Chloramine and salt. For "most skin diseases," inflammations, sore throat, inflamed eyes and dandruff. Fraudulent therapeutic claims.—[*N. J. 25807; January 1937.*]

Red Cross Brand Periodic Pills.—Ernest E. Schneider, trading as Snyder Products Co., Chicago. Composition: Iron sulfate, plant material including a laxative, and a preparation of ergot, coated with sugar and chalk. Fraudulently represented as a "female regulator."—[*N. J. 25826; January 1937.*]

Voxol.—John H. Vernet, trading as Voxol Laboratories, Oak Park, Ill. Composition: Essentially a fixed oil containing volatile oils, including eucalyptus and menthol. For sinus disorders, asthma, pneumonia, diphtheria, etc. Fraudulent therapeutic claims.—[*N. J. 25825; January 1937.*]

Kavatone Soft Mass Pills.—Gray's Medicine Co., South Bend, Ind. Composition: Essentially plant drugs, including a laxative. For gallbladder and liver troubles, etc. Fraudulent therapeutic claims.—[*N. J. 25810; January 1937.*]

Hygena.—Lee W. Wiggins, trading as Hygena Laboratories, Atlanta, Ga. Composition: Essentially epsom salt, boric acid and ammonium alum, perfumed with volatile oils, including peppermint. Not antiseptic as claimed. Fraudulently represented as a remedy for sore feet, inflammation, wounds, hemorrhoids, leukorrhea, etc.—[*N. J. 25827; January 1937.*]

Congoin.—Congoin Co., Los Angeles. Composition: The leaves of yerba maté, a caffeine-bearing plant. Fraudulently represented as supplying necessary minerals lacking in foods, and as a remedy for mental strain, acid stomach, neuritis, rheumatism, etc.—[*N. J. 25833; January 1937.*]

An-Idin.—Hygienic Supply Co., Loudonville, N. Y. Composition: Essentially an iodine compound incorporated in petrolatum, and perfumed with wintergreen. For sciatica, enlarged glands, arthritis, etc. Fraudulent therapeutic claims.—[*N. J. 25834; January 1937.*]

Snyder's (S. P.) Tablets Prescription No. XX.—Ernest E. Schneider, trading as Snyder Products Co., Chicago. Composition: Iron sulfate, plant material including a laxative, and a minute amount of alkaloid, coated with sugar and chalk. Fraudulently represented as a remedy for obstinate and abnormal delayed cases of menstruation.—[*N. J. 25826; January 1937.*]

Pfeiffer's Sore Throat Remedy.—S. Pfeiffer Mfg. Co., St. Louis. Composition: Water, glycerin, ammonium chloride, potassium chlorate and sodium benzoate, with wintergreen flavor. For tonsillitis, hoarseness, ulcerated sore mouth, etc. Fraudulent therapeutic claims.—[*N. J. 25836; January 1937.*]

Kompo Bile Salts Tablets.—Kompo Co., Atlanta, Ga. Composition: Small proportions of iron, calcium and magnesium compounds, bile acid, extracts of plant drugs and phenolphthalein (approximately ½ grain per tablet). Fraudulently represented as a remedy for headaches, indigestion, liver and kidney disorders, gallstones, heart trouble, cancer, etc.—[*N. J. 25829; January 1937.*]

Correspondence

MENTAL DISTURBANCES FROM ATROPINE OR NOVATROPINE GIVEN TO SUBJECTS UNDER THE INFLUENCE OF INSULIN

To the Editor:—Though Dr. J. P. Quigley's article (THE JOURNAL, October 23, p. 1363) is of value in offering pharmacologic evidence for the clinical effectiveness of belladonna derivatives in idiopathic hypoglycemia, his "warning against the administration of atropine preparations" in these conditions, based on observations interpreted as delayed synergistic action, is not justified. Aside from the facts that idiopathic hypoglycemia, most frequently, is not due to hyperinsulinism, and that the transitory beneficial action of belladonna derivatives on hypoglycemic manifestations would naturally be followed by an aggravation of the preceding condition as the effect of the drug wore off, doses of atropine or novatropine respectively greater than 1/100 grain (0.65 mg.) or 1/25 grain (2.5 mg.) under no circumstances can be considered "moderate." When average doses of belladonna derivatives by mouth are not infrequently followed by dryness and dilatation of the pupils, surely subcutaneous doses of atropine as large as 1/60 grain (1.8 mg.) or 1/20 grain (3.5 mg.) of novatropine may be expected to be followed, not infrequently, by symptoms of atropinism, even in conditions not characterized by hypoglycemia.

JOHN F. QUINLAN, M.D., San Francisco.

PORTABLE APPARATUS FOR PROLONGED ARTIFICIAL RESPIRATION

To the Editor:—Dr. Flagg in a communication published in THE JOURNAL, October 9, page 1216, writes concerning patients with poliomyelitis requiring respirator treatment but who are in communities where respirators are not available. He suggests laryngoscopy, intubation and insufflation of oxygen under pressure as a practical means of tiding such patients over this fatal period. He further states that "injuries directed to personnel interested in the care of such cases reveals that the technic has not been used and is not being used."

A portable apparatus for prolonged artificial respiration was devised (Brahdy, Leopold, and Brahdy, M. B.: *Am. J. M. Sc.* **178**:405 [Sept.] 1929) and used at the Willard Parker Hospital before the present type of respirator became available. When artificial respiration in a respirator is advocated, it should be stated that this treatment sometimes has serious and fatal sequelae (Brahdy, M. B., and Lenarsky, Maurice: *J. Pediat.* **8**:429 [April] 1936). Patients with mild or even moderate respiratory embarrassment usually can be tided over their critical period by sedation and reassurance. This phase of the management of poliomyelitis was discussed in an editorial in THE JOURNAL (Dec. 23, 1933, p. 2053).

M. BERNARD BRAHDY, M.D., Mount Vernon, N. Y.

GONORRHEAL ARTHRITIS IN INFANCY

To the Editor:—May I direct the attention of Drs. S. J. Hoffman and Maurice Schneider (Gonorrheal Sepsis in an Infant, THE JOURNAL, October 30, p. 1447) to a report by M. B. Cooperman (Gonorrheal Arthritis in Infancy, *Am. J. Dis. Child.* **33**:932 [June] 1927). This report covers an epidemic of gonococcic infection involving sixty-seven (of 182 new-born infants exposed). Of the sixty-seven infants, fifty-three developed joint infections, the remainder mucous membrane involvement. Forty-four of these infants (twenty-one boys, twenty-three girls) were observed by Cooperman. One infant developed gonorrheal ophthalmia on the sixth day. Otherwise first symptoms were not noted until the eighth or ninth day after exposure (i. e., after birth); elevated temperature, toxic rash, polyarthritis and superficial abscesses. By the eleventh day, diarrhea with purulent stools, and vulvovaginitis were noted. The only positive blood culture obtained, and this after ten days' incubation, was in a boy with polyarthritis. Five boys and three girls had a gonococcic proctitis with positive rectal smears. In no case was there evidence of heart, kidney or lung involvement, and there were no deaths.

A bacteriologic study of a purulent stool early in the epidemic might have disclosed the identity of the organism on the rampage ten days before its initial identification in joint exudate. Writers seem to be minimizing the rectum as a portal of entry for the gonococcus. This possibly is applicable also to the umbilical vessels.

NATHANIEL HURWITZ, M.D., Philadelphia.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

LEUKOCYTE COUNT IN ALLERGY

To the Editor:—I should like information on the value of the leukocyte count in detecting allergic reactions to foods. How great is the range in a normal person after ingestion of 8 ounces of milk after a fifteen hour fast? How great a leukopenia signifies anything in an allergic person when given the inciting food? Do you know of any reliable book or article that can be obtained at this time? Should a food that causes an increase (from 100 to 400 per cent increase in the leukocyte count) be taken from a diet list? An increase seems to occur and is soon (thirty minutes) followed by an ill feeling on the part of the patient.

M.D., Arkansas.

ANSWER.—Early French investigations on food anaphylaxis demonstrated that an acute reaction to allergenic foods was accompanied by a pronounced fall in the leukocyte count (Widal, Joltrain). Vaughan believes that this leukopenic response to allergenic foods is a characteristic reaction in food allergy and may be employed in the identification of suspected foods. He believes that a drop of 1,000 or more below the fasting level following the ingestion of the test food is usually indicative of allergy. Three serial counts are made at intervals of thirty minutes following the ingestion of food. A rise in the leukocyte count is of no diagnostic significance.

Two questions have been raised concerning the reliability of this method. First, it has been suggested that blood counting cannot be performed accurately enough for a drop of 1,000 in the leukocyte count to be significant. Second, the work of several investigators has suggested that normally, even without food ingestion, there is too wide a natural fluctuation in the leukocyte count level to make a drop of 1,000 significant. Recent work, however, appears to have invalidated the greater part of these criticisms. Ponder, Saslow and Schweizer (1931) have shown that, if sufficient cells in the chamber are counted (800), the normal blood leukocyte count remains reasonably constant. Bryan, Chastain and Garrey (1935) have shown that even with a smaller number (10 square millimeters on the counting chamber with blood diluted 1:20), counting may be accurately made to within 700 cells. Garrey and Bryan (1935) have reviewed the physiologic factors which influence the leukocyte count. These must be adequately controlled in the determination of the leukopenic index.

The existence of a normal digestive leukocytosis is still a question. Garrey and Bryan conclude from a review of the various contributions on the subject that there appears to be evidence of a postprandial leukocytosis of low degree but that it is due to factors other than digestion itself, such as increased hydrochloric acid in the stomach, distention of the stomach, and the presence of hot or cold substances in the organ.

Details concerning the technic of blood counting are given by Bryan, W. R.; Chastain, L. L., and Garrey, W. E.: *Am. J. Physiol.* **113**: 416 (Oct.) 1935.

Details of the technic of the leukopenic index determination are given by Vaughan, Warren T., *J. Lab. & Clin. Med.* **21**: 1278 (Sept.) 1936.

Physiologic fluctuation in the true leukocyte count is discussed by Garrey, W. E., and Bryan, W. R.: *Physiol. Rev.* **15**: 597 (Oct.) 1935.

ARTERIOSCLEROSIS OBLITERANS IN FEET

To the Editor:—I have a patient, a man, aged 81, whose only abnormality is peripheral vascular occlusion of the toes and feet. There is no evidence of arteriosclerosis of other vessels, as eye vessels and blood pressure and urine are normal. His principal complaint is painful red burning feet, worse at night. There is no phlebitis, and, considering his age, I consider it to be due to arteriosclerosis rather than to Buerger's disease. I should like information on the use of Padutin in this type of case. There is no intermittent claudication. Who makes Padutin, and where is it available? Is it expensive? What is the present status of the passive vascular exercise machines in this type of case? Who makes these machines, and what is their approximate cost?

M.D., Indiana.

ANSWER.—Burning distress in the feet may well be a symptom of decreased arterial circulation caused by arteriosclerosis. However, this symptom may result from other causes, such as peripheral neuritis. It is assumed that the correspondent's diagnosis of arteriosclerosis obliterans is based on the absence of or diminution of pulsations in the chief arteries of the lower extremities, on reduced temperature of the skin of the feet, and on abnormal rubor with dependence and abnormal pallor with elevation of the feet. However, even when such conditions are observed, the distress may be due either to ischemic neuritis produced by the diminished arterial circulation or to some other cause unrelated to the diminution of circulation. Padutin, which is an insulin-free pancreatic extract manufactured by the Winthrop Chemical Company, 170 Varick Street, New York, is not useful in this particular situation but is of value only in the relief of the symptom intermittent claudication. There is no unanimity of opinion relative to the use of the alternating suction and pressure apparatus in treating arteriosclerosis obliterans. It is, however, quite apparent that the enthusiasm for machines of this type has waned decidedly since they were first placed on the market. Whether or not the correspondent's patient would be benefited by treatment with one of these machines could be determined only by trial. Approximately 100 hours of treatment should be given each extremity. The subject is reviewed by E. V. Allen and G. E. Brown in THE JOURNAL, Dec. 21, 1935, page 229. Machines can be bought from the Cincinnati Scientific Company of Cincinnati, the Warren E. Collins Company of Boston, the J. H. Emerson Company of Cambridge, Mass., or the Burdick Company of Milton, Wis. The cost varies with the type of machine purchased but most of them cost in the neighborhood of $500.

MERCURIAL DIURETICS

To the Editor:—1. In a patient with obstinate edema from progressive heart failure, a mitral valve lesion and myocardial degeneration, what would be considered absolute contraindication to the use of the mercurial diuretics? What is the influence of nephritis and low kidney function? 2. Has it been ascertained or is it accepted that salyrgan is less toxic than novasurol?

M.D., Arkansas.

ANSWER.—1. Although the clinical information given does not suffice for an accurate etiologic diagnosis of the cardiac disease, it may be stated that heart failure per se is certainly not an absolute contraindication to the use of the organic mercurial diuretics. It is assumed, however, that the patient has already received an adequate amount of digitalis, has been on a cardiac diet and has otherwise been given the full benefit of the accepted treatment for heart failure. It is generally agreed that patients with severe myocardial insufficiency should not be given mercurial diuretics before the ordinary measures have been instituted and found to be inadequate in ridding the patient of edema. Contraindications to the use of mercurial diuretics are acute or active (hemorrhagic) chronic glomerulonephritis; low renal function of any origin, e. g., less than 30 to 40 per cent of the average normal urea clearance, inability to concentrate the urine to a specific gravity of 1.018 or higher, or an excretion of less than 25 to 30 per cent of phenolsulfonphthalein in two hours after intravenous injection of the dye; stomatitis, ulcerative lesions of the gastro-intestinal tract, or severe diarrhea; known idiosyncrasy to the mercurial compound; acute or subacute hepatitis with jaundice; cachectic or marantic states; leukemia in the later stages; severe anemia, especially if due to or associated with intestinal hemorrhage; recent coronary thrombosis or severe angina pectoris; failure to obtain diuresis, or the development of oliguria, increased microscopic hematuria, or any other signs of mercury poisoning, after the injection of trial doses of the organic mercurial.

2. In spite of considerable investigation on men and laboratory animals, the comparative toxicity of salyrgan and merbaphen (novasurol) has not been clearly established. The clinical reports indicate that merbaphen is much more toxic than salyrgan. In fact, the latter drug has almost entirely replaced the former in clinical use during the last few years. It should be noted, however, that salyrgan was introduced after enough experience had accumulated in the use of merbaphen to teach physicians the proper indications, contraindications and dosage of this powerful drug. Hence fewer toxic reactions have resulted from the use of salyrgan. Experiments on rabbits showed only slightly more toxicity of merbaphen than of salyrgan (Johnstone, B. I.: *J. Pharmacol. & Exper. Therap.* **42**:107 [May] 1931). Both compounds produced renal lesions typical of poisoning with inorganic mercury. It is possible that the organic radical of merbaphen, apart from the mercury, may be responsible for some toxicity in man. There is no clearcut evidence at present.

LEUKORRHEA

To the Editor:—A white woman, aged 26, single, weighing 105 pounds (48 Kg.), has had a leukorrheal discharge for the past three years, beginning with a slight discharge before and after each menstrual period. At that time she was examined by a physician, smears were taken, and there was no evidence of gonococci being found. She was given 1: 10,000 potassium permanganate douches for approximately four months, which did not seem to help at all. She was advised by another physician later to take Davegan tablets, followed by a cleansing douche. This treatment was taken for a few months with no help. She went to another physician and was given quinine capsules as vaginal suppositories for Trichomonas vaginalis. This also did not help. Again, on the advice of another physician, she was advised to take diluted solution of sodium hypochlorite, which seemed to help best of all. The patient came under my care approximately three months ago. At that time the Wassermann reaction was negative; catheterized urine specimens were negative; the red blood cell count was 4,500,000, the hemoglobin 90 per cent; the white blood cell count 14,400, polymorphonuclears 78 per cent, segmented forms 73 per cent, nonsegmented 75 per cent, lymphocytes 16 per cent, monocytes 6 per cent and eosinophils 1 per cent. Three other white blood counts ranged from 12,000 to 15,000. There has been no elevation of temperature. On pelvic examination a medium sized speculum was inserted with comparative ease. There was first degree retroversion. The uterus was normal in size and consistency, with no evidence of any erosions. There was a seropurulent discharge coming from the cervix. The entire vaginal vault was filled with a white, foamy, purulent discharge, resembling that of Trichomonas vaginalis. The adnexa were completely normal. The vagina was red and inflamed, with a very slight evidence of excoriation. Smears for gonococci were negative. Cultures taken on Sabouraud's medium were negative; agar nutrient medium, 2 Hay bacillus colonies; beef of agar medium, negative; bactodiphtheria culture medium negative; nutrient broth medium, Hay bacillus. The patient was kept in bed for two weeks and given cleansing douches of salt and soda without any relief. April 9, 1937, the vaginal wall was washed with tincture of green soap. This was painful for the patient and on the following day, when she came back for another treatment, the discharge had become white, thick and creamy. The vaginal wall was much too irritated for another treatment of this sort. Menstruation is regular, with a profuse discharge, and slight pain for the first two days. Kindly suggest diagnosis and treatment. Would you advise cauterization of the cervix?

M.D., Florida.

ANSWER.—Trichomonas vaginalis is mentioned a number of times in the query but there is no definite statement as to whether or not this organism was actually found. The simplest and cheapest way to find this out is to examine a drop of the discharge without any staining. A drop of saline solution is added to a drop of the vaginal discharge and the mixture is examined first with the low and then with a high power lens of a microscope. If trichomonads are present, they will be detected with ease because of their motility. The slide should also be studied for Monilia, especially because of the change in the discharge to a white, thick, creamy consistency after treatment with green soap. The appearance of the vagina may be due to excessive and perhaps rough treatment.

The cervix should by all means be treated if it is certain that the seropurulent discharge originates from this structure and is not simply some of the vaginal discharge deposited on the cervix and on the external os. One of the most satisfactory ways to treat the cervix is by means of the nasal tip electric cautery.

Not infrequently in cases in which it is difficult to cure a persistent leukorrheal discharge there is some constitutional disturbance. In some cases the administration of thyroid is distinctly helpful. However, before thyroid is given, it is advisable to have a basal metabolism study.

The treatment of Trichomonas vaginalis vaginitis is unsatisfactory chiefly because recurrences are common. Since the vagina is badly irritated at the present time, it is best to use a dry form of treatment. With great gentleness the vaginal discharge should be removed with cotton pledgets. Then a powder should be blown into the vagina. Satisfactory results are being obtained with sodium methylenesulfonaminohydroxyphenylarsonate, as recently described by Bland and Rakoff (*Am. J. Obst. & Gynec.* **32**:835 [Nov.] 1936; abstr. THE JOURNAL, January 9, p. 145). Biskind (*Lancet* **2**:1049 [Nov. 9] 1935) reported good results following the use of solutions of basic phenylmercuric nitrate. Silver picrate also is recom-

mended. If Monilia is found it can readily be eliminated by the use of gentian violet.

The physician should discuss with the patient the matter of cleansing herself after bowel movements. Many women use an upward sweep from the anus toward the vagina. If trichomonas gains access to the vagina from the rectum, as some individuals believe, such upward sweeping motions may produce reinfections. Patients should be instructed to use a sweeping motion directed away from the vagina and toward the sacrum.

CAUSES OF ACNE

To the Editor:—In mild cases of acne vulgaris the following seems to be the sequence of events: 1. The skin becomes soft, both subjectively and objectively. 2. The skin then becomes relaxed or toneless. 3. At this time it will be noticed that the pores are enlarged and comedones are apparent. 4. The skin assumes a blotchy appearance, and the various forms and phases of the eruption appear. The basic change that seems to have occurred is the relaxation or loss of tone of the skin. If at any time some procedure is carried out that will prevent this relaxation or increase the tone of the skin, the steps will reverse themselves and the skin tend to clear, except for the comedones or pustules that have developed too far. Three procedures that tend to do this are: 1. Applications of medicaments containing sulfur, resorcin, and so on. 2. Application of ultraviolet rays or sunshine. This must be intense enough to cause a sunburn, and the effect is of value only when this reddening sunburn is present; in other words, when and while the patient actually feels the burn. After the skin becomes tanned, the treatment is much less effective or entirely ineffective. Here it will be noted that when the treatment is effective the patient has the feeling that his skin is drawn tight across his face. Examination will reveal the pores to be very small. Under the optimal conditions this treatment will change the course of events and the appearance of the skin over a period of six hours. 3. Application of cold—rubbing ice on the face, exposing the face to cold winds, and the like. Here also the patient will have the feeling that the skin is drawn tight on his face, and it will be noted that the pores of the skin are small. However, under optimal conditions this is not as effective as the ultraviolet rays or sunshine. It is this last observation about which the present communication is concerned—the prophylactic and therapeutic effect of cold on acne vulgaris and its relation to the physiologic cause of the condition. It would seem that the accuracy of this observation might be determined in part, at least, by determining the prevalence of acne vulgaris in the arctic and antarctic circles. (I have never seen a picture of an Eskimo with this condition.) Some of the statements that I have made are subject to dispute, but they are stated dogmatically to develop the point more easily.

E. W. GROVE, M.D., Gainesville, Ga.

ANSWER.—The discussion of the factors in the genesis of acne on the basis of the correspondent's observations is interesting.

The soft, relaxed, toneless skin seen in acne is usually a part of the sluggishness that exists in some of these affected persons at the age of adolescence because of sedentary habits, dietary indiscretions and certain underlying endocrine factors. Any application that tends to combat or alter these factors is usually associated with some degree of improvement. The application of stimulating local applications containing sulfur and resorcinol, the use of erythema doses of ultraviolet rays, or exposure to the sun tends to have a stimulating effect with associated increase in circulation of the skin of the face. The application of cold, because of its astringent effect and subsequent hyperemia, produces the general effects described. Contrast applications with hot and cold water, associated with brisk rubbing of the face, have long been a part of the regimen of therapy in the hands of many.

The type of life led by the inhabitants of the arctic is one of great physical activity in which the people alternate between fast and famine. The diet includes meat and fish of various types obtained from the inhabited regions, which is usually eaten raw. "Contrary to general opinion, the Eskimo eats relatively little fat or blubber" (Thomas, W. A.: Health of a Carnivorous Race: A Study of the Eskimo, THE JOURNAL, May 14, 1927, p. 1559).

A vigorous life with exposure to the elements and the lack of certain excesses in diet is an important contributory factor in the absence of an "acne soil" in the Eskimo.

GASTRO PHOTOGRAPHY

To the Editor:—I would appreciate your opinion of the Gastro-Photo, which has been exhibited at the annual session of the American Medical Association and also some of the state meetings.

W. L. CASLER, M.D., Marquette, Mich.

ANSWER.—Many attempts have been made to develop a direct, anatomic diagnostic procedure for gastric lesions. Three methods exist at this time: (1) the x-ray relief method with compression, (2) gastroscopy and (3) gastrophotography. The x-ray relief method, developed by Forsell and Berg, has been shown to be of great value, especially in the diagnosis of gastric ulcer and tumors, but the smaller lesions, especially the different forms of gastritis and small superficial ulcerations, often cannot be demonstrated in this way. Gastroscopy, developing slowly from 1868, became a safe procedure with the invention of the flexible gastroscope in 1932. The results are excellent. The method should not be confused with open tube procedures such as esophagoscopy. Gastrophotography was initiated first by Lange of Munich in 1898 and reached a certain perfection with the construction of the "gastrophotor," by Back and Heilpern of Vienna in 1929. A small photographic camera, containing eight films which are exposed through "pinhole openings" without lenses, and a lamp are introduced into the stomach. A quick exposure of the eight films is made by pressing a button and thus illuminating the mucosa by the powerful lamp. The results of the three methods have been compared by three gastroscopists, Henning, Moutier and Schindler. All three agree on the great value of the x-ray relief and gastroscopic methods, both of which are considered indispensable and supplementary to one another. On the other hand, these three authors unanimously reject gastrophotography for a number of reasons, the most important of which are: (*a*) the pictures often are blurred, (*b*) a real orientation within the stomach is impossible, and (*c*) the important color changes in the mucosa are not reproduced in the black and white film. Gastrophotography apparently is carried out in a routine way only by Rehfuss in Philadelphia, Heilpern in Vienna, Bernay in Lyons and Hofmann in Buenos Aires, while the other two methods are carried out in many hospitals and clinics all over the world.

SURGERY IN AMYOTROPHIC LATERAL SCLEROSIS

To the Editor:—A patient with diabetes always under control for seventeen years, developed two years ago a spinal lesion situated just above the sixth dorsal rib and manifested by great pain in the extremities. All tests (x-ray, lipoid injection, Queckenstedt's test) were negative and failed to reveal the exact nature of the trouble—whether tumor or hemorrhage. Three months ago she began to display all the symptoms of hyperthyroidism, pulse 120 and the basal metabolism reaching plus 60 per cent. Simultaneously the neurologist changed his diagnosis from a spinal lesion to probable amyotrophic lateral sclerosis. Compound solution of iodine and two months of rest brought the pulse down to 100 and the basal metabolism to plus 35 per cent. A thyroidectomy, or at least a lobectomy, was considered, but it was opposed on the ground that patients with spinal disease, especially amyotrophic lateral sclerosis, cannot withstand the strain of even the most minor operation and usually die. Accordingly, as a last resort, two x-ray treatments were administered. Although the metabolic rate fell to plus 26 per cent, the causal connection between the x-ray treatments and the drop in basal rate is questionable. The problem of the feasibility of a lobectomy has arisen again. Can you throw any further light on the risk involved? The patient, who is about 60 years old, lost little if any weight prior to the onset of the hyperthyroidism and has lost about 30 pounds (13.6 Kg.) since. If an operation is decided on, what anesthetic, in view of the inadvisability of using a spinal anesthetic, would you suggest?

SAUL MEBEL, M.D., New York.

ANSWER.—There is no known evidence that amyotrophic lateral sclerosis is a contraindication for surgical intervention. In this case the only contraindication would be the diabetes. If the latter was well controlled, surgery could be done. Amyotrophic lateral sclerosis is one of the most common causes of true bulbar palsy. When bulbar palsy exists, any anesthetic other than local would be a potential danger because in bulbar palsy the circulatory, respiratory and deglutition functions are defective and anesthesia might make them worse. If the patient has no signs of bulbar palsy, local, nitrous oxide gas, ether or ethylene anesthesia may be used.

METHYL CHLORIDE POISONING

To the Editor:—What is the latest treatment for poisoning from the use of methyl chloride in refrigerators?

M.D., Astoria, N. Y.

ANSWER.—The injury produced in methyl chloride poisoning may represent a profound asphyxiation if the exposure is severe, or it may be substantially the same as that caused by methyl alcohol if the patient escapes or survives asphyxiation. In asphyxiation, the patient should be removed from further exposure, and if respiration has ceased but the victim is still alive, artificial respiration should be carried out. The use of oxygen with or without the addition of 5 or 7 per cent carbon dioxide may be indicated. The objective in this phase of the treatment naturally is to remove from the lungs all possible methyl chloride.

Methyl chloride taken into the body is decomposed into methyl alcohol and hydrochloric acid. Hydrochloric acid combines with mineral salts in the blood to form such substances as sodium and potassium chlorides, which are relatively innocuous, and as a result these salts do not enter into the general poisoning. The treatment for poisoning from methyl

chloride then becomes the same as for poisoning from methyl alcohol. A primary objective is to combat acidosis. In acute situations, intravenous administrations of an alkalizing solution are in order. Administration by mouth and by rectum of similar substances are advised. Enemas of 3 per cent sodium bicarbonate with 5 per cent dextrose solution have been utilized. At times sedatives may be required because of convulsive attacks, but more often respiratory and cardiac stimulants may be applied. The chief points of injury are likely to be the kidneys, the liver and the central nervous system, including the optic nerves. For their protection, treatment should be directed to the prompt elimination of the methyl alcohol, which is discharged from the body much less readily than ethyl alcohol.

ABDOMINAL CRISES

To the Editor:—A German, aged 50, well developed and of good nutrition, for the past thirteen years has had recurring attacks of pain in the right upper quadrant of the epigastrium. These pains start gradually and increase in intensity for about four to six hours until they are severe and then gradually subside. They are gone in from eighteen to twenty-four hours, leaving him in perfect health again. While the pains are present, they are constant and are relieved only by opiates. The interval between attacks has always been well defined. At first it was about twenty days. A few years ago it changed to eleven days, and at present it recurs at nine day intervals. The patient can predict the day on which it will come. During the years of his illness he has been seen by numerous gastro-enterologists. He has been roentgenographed and given gastric function tests. All tests were negative. The Wassermann reaction was negative. Nevertheless, on one occasion several years ago a surgeon was convinced that the trouble lay in the gallbladder. He did a cholecystectomy. The pains continued as before. Physical examinations show no tenderness or other abnormalities. The man was told by several gastro-enterologists that nothing could be done for him. Have you any suggestions to offer?

M.D., New York.

ANSWER.—It is impossible to arrive at an exact diagnosis from the evidence presented. In spite of the fact that the Wassermann reaction was negative, it might be interesting to know the results of the Kahn reaction of the blood and the serologic reaction in the spinal fluid. These abdominal crises are not at all uncommon in syphilis and malaria and often have been known to occur as abdominal manifestations of epileptiform seizures. In the latter connection, these attacks are frequently relieved by putting the patient on a ketogenic diet and giving small doses of phenobarbital. Other than that there are no suggestions to be made.

NONSPECIFIC URETHRITIS

To the Editor:—Two evenings ago a patient had had intercourse with his wife for the first time in two weeks. He used a condom, known as "Gold-Tex." Shortly after the emission he noted some burning within the urethra. The next day it was worse. That evening (the one following the intercourse) he noted some white discharge. This was greater in amount the following day. Examination showed pus on the end of the penis. The first glass was cloudy with shreds, the second clear with shreds. Microscopic examination showed many pus cells with no organisms on two successive days. He stated that he had not had extramarital contact during the past year. There is no previous history of infection. He had used four of the same type prophylactics two weeks previously without difficulty. This type condom has what looks like yellow or gold powder at the tip (inner). After three days' treatment the pus disappeared, although the first glass appeared slightly cloudy with shreds. Burning on micturition had ceased. Are there any records of a nonspecific urethritis caused by "Gold-Tex" condoms? Does this not appear more of a nonspecific than a gonorrheal urethritis?

M.D., Connecticut.

ANSWER.—If the gonococcus could not be demonstrated in this case, it is evidently a case of nonspecific urethritis. Rubber condoms may be the cause of dermatitis, balanitis and nonspecific urethritis. The people who develop these conditions are those who are sensitive to rubber. Such cases have been reported in the literature (Obermayer, M. E.: Eczema Due to Hypersensitiveness to Rubber, *Arch. Dermat. & Syph.* **17**:25 [Jan.] 1933. Rattner, Herbert: Dermatitis of the Penis from Rubber, THE JOURNAL, Oct. 12, 1935, p. 1189).

IODIDES IN TUBERCULOSIS—RAISING ARMS IN TUBERCULOSIS

To the Editor:—Two questions in tuberculosis: 1. Is the aversion to iodides sound or is it based on the questionably analogous action in gummas? 2. Some men forbid patients to raise their arms above the head. Is this sound or a fetish based on faulty anatomic reasoning?

M.D., New York.

ANSWER.—1. Considerable doubt has arisen in the minds of physicians as to whether iodides in usual dosage have any deleterious effect on the lesions of pulmonary tuberculosis. At one time the iodides were used extensively in the diagnosis of pulmonary tuberculosis; that is, when tubercle bacilli could not be recovered from the sputum large doses of iodides were administered, following which in some cases tubercle bacilli appeared in the sputum. The conclusion was drawn that the iodides broke down the lesions and liberated bacilli. As these drugs serve as expectorants by increasing and liquefying the secretions in the bronchial tree, it seems probable that they only resulted in liberation of mucus and other materials from the region of the lesion in which bacilli could be demonstrated. The fear of the administration of iodides to tuberculous patients has definitely decreased in the past few years.

2. There is also considerable doubt whether forbidding patients to raise their arms above the head has any sound basis. The most that can happen by bringing the arms to this position is a slight elevation of the ribs to which the pectoral muscles are attached, but this probably is not as great as, or certainly no greater than, the elevation of the ribs on ordinary inspiration. Like a number of beliefs with no scientific basis, coincidence was probably responsible for this one. For example, a patient may have a pulmonary hemorrhage begin while the arms are above the head and the conclusion is immediately drawn that it was this position which resulted in the hemorrhage, when in reality it would have occurred regardless of the position of the arms.

DERMATITIS FROM HAIR DYE

To the Editor:—A middle-aged woman about nine years ago and again recently developed a dermatitis following the use of hair dye to blacken her hair. The first time both eyes were swollen and the scalp was red, but the condition did not last long. The last time, within twenty-four hours after visiting a beauty parlor, her scalp began to itch and burn and her eyes began to swell, which progressed to complete closure of both eyes. This condition lasted about twelve hours. During this time her scalp was red and edematous, the edema and redness extending below the hair line and down the back of the neck. I saw her again yesterday, ten days after the dye was applied, and the scalp, in spots and all around the hair line extending over the temples and the back of neck, was cracked, and there were dry crusts between, with serum pouring from the cracks. I have used hot physiologic solution of sodium chloride and calamine lotion after an initial shampoo to begin with. The eyes are still a bit puffy but otherwise the physical examination, including urinalysis, was negative. She does not recall the brand of the hair dye she first used, but the last was called "Cloral Hair Dye," made or distributed from Danville, Ill. She is anxious to avoid a repetition of this experience, and I should like to know what was probably the causative drug or drugs. Her general health is good and she shows no allergic symptoms.

M.D., Indiana.

ANSWER.—The common offender in hair dyes is paraphenylenediamine, an efficient black dye. No information as to the composition of "Cloral" dye is obtainable. The patient, to avoid future trouble, will have to stop dyeing her hair. Hairdressers cannot be depended on to know what is in the dyes, and paraphenylenediamine is so much more satisfactory than any other dye that she is sure to have it used again if she continues having her hair dyed.

VARICOCELE

To the Editor:—Kindly outline the present day treatment of varicocele. Is operation performed as much as formerly? If so, what is the type of operation? To what extent is varicocele a bar to employment in industry? Is it now considered a forerunner of hernia?

M.D., Minnesota.

ANSWER.—A varicocele is not operated on frequently. It occurs in adolescence and its symptoms, which may be to a certain extent mental, usually subside in a few years. Varicocele usually occurs on the left side but it is occasionally bilateral and when associated with a long dependent scrotum may produce some disability in an active person. In certain industries requiring considerable activity or standing it would be considered a handicap. This would depend on the degree of enlargement of either the varicocele or the scrotum and the symptoms produced, together with the type of work demanded.

Varicocele is not considered as predisposing to hernia.

The development of a varicocele in an older man on the left side should lead one to suspect pressure or neoplasm in the region of the kidney involving the internal spermatic vein, which empties into the left renal vein. Operation for varicocele should never be done at the same time as a hernia operation unless one understands the danger of postoperative atrophy of the testicle from pressure about the remaining veins in the inguinal canal after resection of a portion of the varicose veins. Atrophy is not likely to occur when the operation is limited to the resection of a short segment of only a part of the varicose veins and approximation of their ends to aid suspension of the testicle. The lower portion of a long redundant scrotum may be resected at the same time, but great care should be taken to control bleeding. Following operation there should be no physical disability or handicap in heavy labor.

ECTHYMA OR FACTITIOUS DERMATITIS

To the Editor:—Can you offer any suggestion as to the possible cause of a peculiar lesion on a school girl, aged 15 years, which first appeared to be a blister from a burn, then looked mildly infected, and was dressed with moist antiseptics but took nearly a month to form a firm crust? This, after five weeks, appears as a punched out, nearly healed ulcer three-fourths inch across, with a black, hard, slightly depressed covering. She had a similar smaller lesion on the forearm a year or so ago, which ran a similar course and the same indefinite history of a burn to account for it. She is in good health and has no skin disease of any kind. The only examination was of the urine, which was negative for sugar, albumin, and casts or cells. PAUL W. VANMETRE, M.D., Rockwell City, Iowa.

ANSWER.—The lesion described suggests the diagnosis of ecthyma. The possibility of a dermatitis factitia (self-induced eruption) must also be considered.

Treatment of ecthyma consists in removal of the crusts and the application of 3 per cent ammoniated mercury to the base of the ulcer. Daily painting with 3 per cent aqueous solution of gentian violet is also effective. The description of the origin of the lesion strongly suggests the possibility of an external irritant as a causative factor; while this irritant may result from contact, the possibility of dermatitis factitia in a girl of 15 deserves consideration. Close observation and the use of a fixed occlusive dressing should rule this out.

MÉNIÈRE'S DISEASE

To the Editor:—I am suffering from Ménière's disease. I had the first attack some twenty odd years ago. It lasted an hour or so and was relieved by a narcotic. Since then it has come about once or twice a year. For the last three weeks it has been with me day and night. I have a constant roaring in my left ear. I am deaf and cannot move my eyes without holding on to something for support, else I fall. Please help me. All the remedies suggested by Nebraska specialists have not benefited me. I am 76 years old. M.D., Nebraska.

ANSWER.—There are at least two types of treatment for Ménière's disease: medical and surgical. The medical treatment of his condition is well described by Madelaine R. Brown (THE JOURNAL, April 3, p. 1158). The surgical treatment consists of resecting the vestibular branch of the eighth nerve. This operation is especially recommended by Dandy. While there is some dissenting opinion as to the efficiency of surgical intervention, in this particular instance with the symptoms as severe as described, and granted that the diagnosis is correct and that the treatment so far is modern, resection of the vestibular portion of the eighth nerve under local anesthesia would appear to be a proceeding that offers the most hope and with no undue risk, even considering the age of the patient.

IODIDES IN RESPIRATORY INFECTIONS

To the Editor:—Will you render me a critical opinion regarding the use of iodides in the treatment of acute respiratory infections? There is a tendency on the part of many physicians to use calcium iodide (calcidin), sodium iodide, organidin, hydriodic acid and the like during the acute phases of respiratory infections. Is this sound therapy? Some investigators seem to feel that iodine may increase edema and dissolve nature's protective barriers and that its use should be withheld until the afebrile period, when it may aid in promoting absorption of the residue. I have felt that iodine may be harmful if not judiciously used.

M.D., California.

ANSWER.—It is perfectly correct that iodides are not suitable in acute stages of infections of the upper respiratory tract, as they are likely to aggravate existing congestion and irritation. They are even charged with the tendency possibly to produce glottis edema, when given in such cases. It is in subacute and most especially in chronic conditions that iodide is so very useful.

ATROPHY OF TESTIS

To the Editor:—I am 27 years of age. Five years ago a herniotomy for a right-sided inguinal hernia caused complete atrophy of the right testicle. Six weeks ago a herniotomy on the left side resulted in an epididymo-orchitis. At the present time the left testicle is slightly smaller than it was prior to operation, is extremely hard, and is not tender even to excessive pressure. What is the prognosis as to atrophy? If it does atrophy, what treatment, surgical or medical, will prevent or alleviate the results of castration? M.D., Massachusetts.

ANSWER.—Since there are varying degrees of postoperative atrophy of the testicle, which is rarely bilateral, one cannot predict the extent of loss of function without further studies on the presence of hormones and spermatozoa under these conditions.

Atrophy of the testicle with absence of spermatozoa following a traumatic or postoperative orchitis will rarely involve the interstitial cells; consequently the symptoms of castration should not occur and endocrine therapy would be unnecessary.

At the meeting of the Chicago Society of Internal Medicine, January 25, Fred C. Koch reported a rapid method for quantitative extraction of the sex hormones in normal men and women.

The presence of an epididymitis would temporarily and perhaps permanently prevent the passage of spermatozoa, even if present.

One should search for spermatozoa and, if absent for some time following a preexisting epididymitis, surgical anastomosis of the efferent ducts of the testicle or the lobules of the epididymis to the ductus deferens on that or even the opposite side might be performed to short circuit an obstructed segment, if spermatozoa can be found above it at operation or by aspiration of a spermatocele.

DANGERS OF BUTYN IN URETHRA

To the Editor:—E. B., aged 40, colored, was admitted to the hospital for treatment of acute retention due to multiple urethral strictures. General physical examination was entirely negative otherwise. Attempts to catheterize with metal and rubber catheters were in vain, and there was considerable trauma attendant on such attempts. However, the patient succeeded in voiding following the use of prolonged sitz baths. The following day a large amount of 4 per cent butyn (10-15 cc.) was injected with some force into the urethra and a bougie was inserted but could not be made to pass the final stricture. On the next day, immediately following a hot sitz bath an hour long, the injection of 1 drachm (4 cc.) of 4 per cent butyn resulted almost immediately in convulsions of a generalized clonic type, which subsided, only to be resumed again in a few minutes; breathing became increasingly difficult, the lungs filling with a moisture, and the patient died in less than five minutes. The blood nonprotein nitrogen immediately after death was 29 mg., and spinal fluid also withdrawn immediately after death showed no cells or globulin, and the Kahn and Wassermann reactions were negative. Permission was not obtained for a postmortem examination. Please let us know your opinion of this case.

M.D.

ANSWER.—Butyn is more toxic than certain of the other local anesthetics; the fatality in this case, however, should not be attributed to butyn any more than to another local anesthetic that might have been administered. The Council on Pharmacy and Chemistry and THE JOURNAL have warned against the use of local anesthetics in the presence of trauma, many times. The circular issued by the Abbott Laboratories and accepted by the Council contains the following statement:

"IN GENITO-URINARY SURGERY: *When trauma exists the use of any local anesthetic is contraindicated.*"

ATOPIC ECZEMA

To the Editor:—I have under my care a child, aged 2 years, who has had an eczema-like skin eruption almost since birth, in the region of the elbows and in both inguinal regions. On physical examination the patient is a perfect specimen of health. All laboratory examinations have been negative. The patient comes from healthy stock with a history of allergy on the mother's side. A thorough skin testing of the child with all material available shows very strong reactions to the different kinds of nuts, which the patient has never eaten, according to the parents, who are very careful and intelligent. Could this chronic eczema have anything to do with the child's sensitiveness to nuts? If not, what would you advise as to the proper procedure in treating this condition? M.D., Kansas.

ANSWER.—With the hereditary, allergic background, and an eruption of "eczema-like" character, this case is most probably an atopic eczema. Even though the patient does not eat nuts, the presence of related nut substances in vegetable fats (margarine, coconut oils, and the like) may be a source of nut substances. The complete elimination of anything that may contain nuts or their derivatives in view of the patient's positive reaction must be assured. A regimen with careful diet elimination should be instituted. Soothing local applications, ultraviolet exposures and dicalcium phosphate by mouth, together with vitamins A and D, constitute a valuable adjunct to other management.

HEMOSTATICS IN HEMORRHAGE

To the Editor:—Will you please inform me as to the value of hemoplastin (Cutter's) or similar products in the control of hemorrhage from the lung caused by injury to the chest in an automobile accident? What is the opinion as to the value of calcium chloride intravenously in such a case to arrest hemorrhage? The patient prior to the accident was a perfectly well young adult. M.D.

ANSWER.—Pickering and Hemmingway demonstrated beyond question that hemostatics definitely shorten the coagulation time of shed blood. This does not prove, however, that the resultant clot is of increased value in closing bleeding vessels. Evarts Graham makes no mention of the use of drugs in the care of intrathoracic hemorrhage resulting from trauma. It is well established that, in the normal healthy person, loss of blood in itself decreases coagulation time and that drugs are of relatively

insignificant value. Although coagulation of blood depends on the action of calcium ions on prothrombin, producing thrombin, there is ample mobile calcium in the normal person so that additional calcium is unnecessary. Intravenous injection of calcium salts carries with it some danger of unfavorable cardiac action.

Transfusion of blood from a suitable donor is the best treatment in such cases, as it provides human coagulating substances in addition to fluid volume and erythrocytes.

CALCIUM DEPOSITS IN TISSUES

To the Editor:—A patient while confined to a hospital was given an intravenous injection of calcium chloride in the arm by an attending intern. The solution went outside the vein and infiltrated the surrounding superficial and deep tissues. After the inflammatory reaction subsided the result was an ugly red scar and multiple lumps of hard calcareous deposits in the tissues. Will you please inform me as to whether there is a way to dissolve the calcium lodged in the tissues and if there is a possibility of its being absorbed in time. M.D., Washington.

ANSWER.—No satisfactory method has been devised for successfully dissolving adventitious calcareous deposits in the soft tissues. Resorption over a long time is possible, but encapsulation is the more common method of foreign body segregation—another reason for the failure of solvents.

The treatment advised after accident is multiple stab punctures and small incisions as soon as possible, attempting to massage the chemical irritant out of the tissues, followed by hot applications of magnesium sulfate. Injection of salt solutions to dilute the chemical is not practical, since the original route of the infiltrating calcium chloride solution cannot be retraced. In addition, the mechanical edema further embarrasses the normal attempts at resorption. In the late stages, after scar and nodule formation, plastic surgery is the only resort.

LATE TREATMENT OF BURNS

To the Editor:—A patient who was severely burned about the face and hands—second and third degree burns—has had complete epithelization but still a great deal of redness in the burned area. Since the termination of the wax dressings, I have been using olive oil and hydrous wool fat locally. The burn is now eight weeks old. What would you suggest to keep the skin soft? Can anything be done to reduce the redness or will this persist until the skin becomes thicker? Some time ago you published a formula for a scarlet red ointment to stimulate epithelization. Will you please repeat this? M.D., Pennsylvania.

ANSWER.—Redness in the healed area following second and third degree burns has a tendency to disappear in time. Keeping the skin soft with olive oil and hydrous wool fat tends to improve the general condition of the superficial scar tissue and the epithelium. Compresses of boric acid solution applied several hours daily have a tendency to reduce the incidence of local infections, which may occur in small fissures. X-rays should not be used in an effort to hasten the disappearance of redness in such areas. There is a difference of opinion as to the value of x-rays in the treatment of keloids. Some dermatologists and radiologists consider them of great value. When used, the treatment should be carefully supervised. Scarlet red is usually applied as a 5 per cent ointment.

GOLD BRIDGEWORK TURNING BLACK

To the Editor:—A patient, employed as a domestic, is apparently in good health but complains that gold bridgework, recently applied, turns black rapidly. What are the possible causes of such a condition, and how may it be remedied? M.D., New York.

ANSWER.—The "gold" bridgework is probably made of a low carat gold. It may be remedied by the use of a higher carat gold.

ZINC IONIZATIONS FOR VASOMOTOR RHINITIS

To the Editor:—What is the clinical value of zinc ionizations for vasomotor rhinitis? M.D., New Jersey.

ANSWER.—Zinc ionization has been recommended for vasomotor rhinitis, and while there are favorable reports there are also many disappointments. Recently reports have appeared from men of good standing indicating that the method may be a severe one; its results are not specific; they depend on the production of local changes of a caustic type in the nasal mucous membrane, and very late unfavorable after-effects are still to be looked for.

References:

Harkness, G. F.: Why I Have Not Used Iontophoresis, *Ann. Otol., Rhin. & Laryng.* **46**: 169 (March) 1937.

Dean, L. W., and others: Allergic Rhinitis, *ibid.* **45**: 101 (March) 1936.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, June 28. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ALASKA: Juneau, March 1. Sec., Dr. W. W. Council, Box 561, Juneau.

ARKANSAS: *Medical (Regular).* Little Rock, Dec. 21-22. Sec., Dr. L. J. Kosminsky, Texarkana. *Medical (Eclectic).* Little Rock, Dec. 21. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

COLORADO: *Basic Science.* Denver, Dec. 15-16. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver. *Medical.* Denver, Jan. 5-7. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Basic Science.* New Haven, Feb. 12. *Prerequisite to license examination.* Address State Board of Healing Arts, 1895 Yale Station, New Haven.

DELAWARE: Dover, July 12-14. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science.* Washington, Dec. 27-28. *Medical.* Washington, Jan. 10-11. Sec., Dr. George C. Ruhland, 203 District Bldg., Washington.

GEORGIA: Atlanta, June. Joint Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

IDAHO: Boise, April 5-6. Commissioner of Law Enforcement, Hon. J. L. Balderston, 205 State Capitol Bldg., Boise.

ILLINOIS: Chicago, Jan. 25-27. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

INDIANA: Indianapolis, June 21-23. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

IOWA: *Basic Science:* Des Moines, Jan. 11. Sec., Dr. W. L. Strunk, Decorah.

KANSAS: Topeka, Dec. 14-15. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 N. 7th St., Kansas City.

MARYLAND: *Medical (Regular).* Baltimore, Dec. 14-17. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Medical (Homeopathic).* Baltimore, Dec. 14-15. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MINNESOTA: *Basic Science.* Minneapolis, Jan. 4-5. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, Jan. 18-20. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MONTANA: Helena, April 5-6. Sec., Dr. S. A. Cooney, 205 Power Block, Helena.

NEBRASKA: *Basic Science.* Omaha, Jan. 11-12. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: *Reciprocity.* Carson City, Feb. 7. Sec., Dr. John E. Worden, Capitol Bldg., Carson City.

NEW HAMPSHIRE: Concord, March 10-11. Sec., Board of Registration in Medicine, Dr. Fred E. Clow, State House, Concord.

NEW JERSEY: Trenton, June 21-22. Sec., Dr. James J. McGuire, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April 11-12. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York, and Syracuse, Jan. 24-27, June 27-30, and Sept. 19-22. Chief, Professional Examinations Bureau, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH DAKOTA: Grand Forks, Jan. 4-7. Sec., Dr. G. M. Williamson, 4½ S. 3rd St., Grand Forks.

PENNSYLVANIA: Philadelphia, Jan. 4-8. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

RHODE ISLAND: Providence, Jan. 6-7. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: Pierre, Jan. 18-19. Director of Medical Licensure, Dr. B. A. Dyar, Pierre.

TENNESSEE: Memphis, Dec. 22-23. Sec., Dr. H. W. Qualls, 130 Madison Ave., Memphis.

VERMONT: Burlington, Feb. 8. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

WISCONSIN: Madison, Jan. 11-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

WYOMING: Cheyenne, Feb. 7. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the *National Board of Medical Examiners* and *Special Boards* were published in THE JOURNAL, December 4, page 1931.

Ohio June Examination

Dr. H. M. Platter, secretary, Ohio State Medical Board, reports the oral, written and practical examination held at Columbus, June 1-4, 1937. The examination covered 10 subjects and included 80 questions. An average of 75 per cent was required to pass. Two hundred and ninety-six candidates were examined, 291 of whom passed and 5 failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Colorado School of Medicine		(1936)	87.8
George Washington University School of Medicine		(1933)	84.2, (1936) 82.9, (1937) 83.9
Georgetown University School of Medicine		(1936)	82.8
Loyola University School of Medicine		(1937)	78.5,* 81.2, 81.4,* 81.5, 81.9,* 86.3,* 86.4*
Northwestern University Medical School		(1937)	80.7

School		
Rush Medical College	(1935)	81.2, (1936) 84.6, (1937) 82, 83.1, 83.8
School of Medicine of the Divison of the Biological Sciences	(1937)	82.6
Harvard University Medical School	(1932)	85.4, (1936) 84.6, (1937) 85.8, 86.6
University of Nebraska College of Medicine	(1932)	82.5
Columbia University College of Physicians and Surgeons	(1937)	84.3
New York Medical College and Flower Hospital	(1937)	83.7
University of Rochester School of Medicine	(1937)	81.9, 83.6, 85.4
Eclectic Medical College, Cincinnati	(1937)	78.2, 79.5, 79.8, 80.2, 81, 81.3, 81.6, 82.9, 83.4, 83.9, 84.1, 84.3, 84.3, 84.7, 85.4, 85.6, 85.8, 86.1, 86.2, 86.4, 86.7, 87.5, 87.9
Ohio State University College of Medicine	(1937)	78.1, 78.7, 78.8, 79, 79.5, 79.5, 79.7, 79.8, 80.1, 80.4, 80.6, 80.7, 81, 81.4, 81.5, 81.6, 81.6, 81.7, 81.8, 81.8, 81.8, 81.9, 82, 82, 82.2, 82.2, 82.3, 82.4, 82.4, 82.4, 82.4, 82.7, 82.7, 82.9, 83, 83, 83.1, 83.1, 83.1, 83.2, 83.3, 83.3, 83.4, 83.4, 83.5, 83.6, 83.7, 83.7, 83.7, 83.8, 83.8, 83.8,† 83.9, 83.9, 83.9, 84, 84, 84, 84.1, 84.1, 84.2, 84.2, 84.2, 84.4, 84.4, 84.6, 84.6, 84.6, 84.6, 84.6, 84.7, 85, 85.1, 85.1, 85.1, 85.2, 85.3, 85.3, 85.4, 85.5, 85.6, 85.7, 86.2, 86.5, 86.6, 86.7, 86.7, 86.8, 87.1, 87.3, 87.7, 88.8, 89.9
University of Cincinnati College of Medicine	(1937)‡	78.6, 78.6, 79.3, 80.1, 80.7, 81, 81, 81, 81.6, 81.7, 81.7, 81.9, 82, 82.2, 82.5, 82.6, 82.7, 82.8, 82.9, 83, 83.1, 83.1, 83.2, 83.2, 83.2, 83.5, 83.6, 83.6, 83.8, 83.8, 83.8, 83.9, 83.9, 83.9, 83.9, 84, 84, 84.2, 84.3, 84.3, 84.4, 84.6, 84.6, 84.7, 84.8, 84.9, 84.9, 84.9, 85.2, 85.2, 85.5, 85.8, 86, 86.1, 86.3, 86.6, 87.5, 87.5, 88, 89, 89.1, 90.6, (1937) 80
Western Reserve University School of Medicine	(1937)	76, 79.4, 79.7, 80.3, 80.6, 80.8, 81.2, 81.3, 81.5, 81.5, 81.7, 81.7, 81.7, 81.8, 81.9, 82, 82, 82.1, 82.1, 82.2, 82.2, 82.3, 82.6, 82.6, 82.8, 83, 83.1, 83.2, 83.2, 83.3, 83.3, 83.3, 83.4, 83.4, 83.4, 83.5, 83.9, 83.9, 83.9, 84, 84.1, 84.2, 84.3, 84.4, 84.5, 84.8, 84.8, 85, 85, 85.1, 85.4, 85.4, 85.5, 85.8, 86.4, 86.6, 86.9, 87.3, 87.6, 88.1, 88.3, 88.6
Hahnemann Medical College and Hosp. of Philadelphia	(1936)	81.5
Jefferson Medical College of Philadelphia	(1935)	84.1, (1936) 80.5, 83.3
Temple University School of Medicine	(1936)	78.5
University of Pennsylvania School of Medicine	(1937)	84.2
Meharry Medical College	(1909)	75.7
Marquette University School of Medicine	(1937)	78.4, 79.6,* 79.8, 83.9, 85.6
Dalhousie University Faculty of Medicine	(1937)	81.4
University of Toronto Faculty of Medicine	(1935)	82.8
Albert-Ludwigs-Universität Medizinische Fakultät, Freiburg	(1924)	83.8§
Hessische Ludwigs-Universität Medizinische Fakultät, Giessen	(1918)	79.4§
Universität Heidelberg Medizinische Fakultät	(1927)	80.9§
Universität Leipzig Medizinische Fakultät	(1925)	75.4§
Regia Università degli Studi di Palermo. Facoltà di Medicina e Chirurgia	(1936)	75§
Université de Lausanne Faculté de Médecine	(1936)	77.4§

School	FAILED	Year Grad.	Per Cent
Medizinische Fakultät der Universität Wien		(1932)	70.2§
Deutsche Universität Medizinische Fakultät, Prag		(1936)	71.8§
Albert-Ludwigs-Universität Medizinische Fakultät, Freiburg		(1917)	71§
Julius-Maximilians-Universität Medizinische Fakultät, Würzburg		(1918)	71.9§
University of Dublin School of Physic, Trinity College		(1937)	73.4§

* This applicant has completed the medical course and will receive the M.D. degree on completion of internship. License withheld until diploma is reviewed.

† License withheld until diploma is reviewed.

‡ These applicants have received the M.B. degree and will receive the M.D. degree on completion of internship.

§ Verification of graduation in process.

North Dakota July Report

Dr. G. M. Williamson, secretary, North Dakota State Board of Medical Examiners, reports the oral, written, and practical examination held at Grand Forks, July 6-9, 1937. Seven candidates were examined, all of whom passed. Four physicians were licensed by reciprocity and four physicians were licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.
Loyola University School of Medicine		(1937)
Rush Medical College		(1937)
University of Minnesota Medical School		(1937, 4)
St. Louis University School of Medicine		(1933)

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
College of Medical Evangelists		(1931)	California
University of Colorado School of Medicine		(1928)	Indiana
University of Illinois College of Medicine		(1915)	Illinois
University of Wisconsin Medical School		(1931)	Wisconsin

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Rush Medical College		(1927)	N. B. M. Ex.
Harvard University Medical School		(1934)	N. B. M. Ex.
University of Minnesota Medical School		(1936)	N. B. M. Ex.
University of Nebraska College of Medicine		(1930)	N. B. M. Ex.

Illinois June Examinations

Mr. Homer J. Byrd, superintendent of registration, Department of Registration and Education, reports the written and practical examination held in Chicago, June 22-26, 1937. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Two hundred and eighty-eight candidates were examined, 286 of whom passed and two failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists		(1937)	84
George Washington University School of Medicine		(1936)	81, 85*
Chicago Medical School		(1937) 78, 79, 79, 80, 80, 80, 81, 81, 81, 81, 81, 81, 81, 82, 82, 82, 82, 82, 82, 82, 82, 82, 82, 83,* 83, 83, 83, 84, 84, 84, 84, 84, 84, 84, 84, 85,* 85,* 85, 85, 85, 85, 85, 85, 85, 85, 85, 86, 86, 86, 86, 86, 87, 89*	76,
Loyola University School of Medicine		(1937) 77, 78, 79, 80,* 80,* 80, 80, 81, 81, 81, 81, 81, 81, 81, 81, 81, 82, 82, 82, 82, 82, 82, 82, 82, 82, 82, 82, 82, 83, 83, 83, 83, 83, 83, 83, 83, 84, 84, 84, 84, 84, 84, 84, 84, 85,* 85, 85, 85, 86,* 86, 86, 86, 87, 87, 87	75,*
Northwestern University Medical School		(1936) 87, (1937) 80, 80, 80, 82,* 82, 83, 83, 83, 83, 83, 83, 84,* 84, 84, 85, 85, 85, 85, 85, 86,* 86,* 86, 86, 87, 87, 90*	79,
Rush Medical College		(1936) (1937) 81, 81, 81, 83,* 83, 83, 83, 83, 83, 84, 84, 85, 86, 86, 86, 86, 86, 87, 87, 87, 87, 87, 88*	81,
School of Medicine of the Division of the Biological Sciences		(1937) 82, 83,	85, 87
University of Illinois College of Medicine		(1935) (1937) 78, 79, 80, 80, 81, 81, 81, 81, 82, 82, 82, 82, 82, 82, 82, 83,* 83,* 83, 83, 83, 83, 83, 83, 83, 83, 83, 83, 83, 83, 83, 84, 84, 84, 84, 84, 84, 84, 84, 84, 84, 84, 84, 84, 85,* 85,* 85, 85, 85, 85, 85, 85, 85, 85, 85, 85, 86,* 86, 86, 86, 86, 86, 86, 86, 87, 87, 87, 87, 87, 87, 87, 87, 87, 87, 87, 87, 88, 88, 88, 90, 91	80,*
Harvard University Medical School		(1932) 84, (1936)	86
University of Minnesota Medical School		(1932)	82
St. Louis University School of Medicine		(1936)	83, 85
Creighton University School of Medicine		(1936)	81, 82
University of Oregon Medical School		(1934) 83, (1935)	81
Woman's Medical College of Pennsylvania		(1936)	86
Marquette University School of Medicine		(1937)	83
University of Wisconsin Medical School		(1935)	83
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin		(1931)	82†
Ludwig-Maximilians-Universität Medizinische Fakultät, München		(1922) 85,† (1932)	78
Universität Heidelberg Medizinische Fakultät		(1924)	78†
National University of Athens School of Medicine		(1930)	80†
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest		(1922)	80†
Universität Basel Medizinische Fakultät		(1936)	82†
Universität Bern Medizinische Fakultät		(1935)	83†

School	FAILED	Year Grad.
Chicago Medical School		(1922)
Universitatea din Bucureşti Facultatea de Medicină		(1934)†

Forty-three physicians were successful in the practical examination for reciprocity and endorsement applicants held in Chicago, June 24. The following schools were represented:

School	PASSED	Year Grad.	Reciprocity with
College of Medical Evangelists		(1930)	California
Rush Medical College		(1934)	Minnesota
School of Medicine of the Division of the Biological Sciences		(1935)	Michigan
University of Illinois College of Medicine		(1932)	Wisconsin
State University of Iowa College of Medicine		(1927), (1932)	Iowa
University of Kansas School of Medicine		(1930), (1932)	Kansas
University of Louisville School of Medicine		(1936)	Kentucky
Johns Hopkins University School of Medicine		(1923)* (1913), (1935)*	Kentucky, Maryland
Harvard University Medical School		(1933)	Wisconsin
University of Minnesota Medical School		(1932),* (1936)	Minnesota
St. Louis Univ. School of Med.		(1933), (1935), (1936, 3) (1935)*	Missouri, Pennsylvania
Washington University School of Medicine		(1932), (1934), (1935),* (1935), (1936, 2)	Missouri
Creighton University School of Medicine		(1930)*	Utah
Eclectic Medical College, Ohio		(1928)*	Ohio
Western Reserve Univ. School of Medicine		(1933), (1934)	Ohio
Hahnemann Med. College and Hospital of Philadelphia		(1936)	Maryland
University of Pittsburgh School of Medicine		(1934)	Penna.
Marquette University School of Medicine		(1936)	Wisconsin
University of Wisconsin Medical School		(1933), (1934)	Wisconsin
University of Manitoba Faculty of Medicine		(1932)	Michigan
University of Edinburgh Faculty of Medicine		(1919)	Nebraska

School	PASSED	Year Grad.	Endorsement of
Northwestern University Medical School		(1930)	N. B. M. Ex.
Johns Hopkins University School of Medicine		(1932)	N. B. M. Ex.
Harvard University Medical School		(1934)	N. B. M. Ex.
University of Minnesota Medical School		(1934)*	N.B.M.Ex.
Washington University School of Medicine		(1930)*	N.B.M.Ex.

* License has not been issued.

† Verification of graduation in process.

Book Notices

Cunningham's Text-Book of Anatomy. Edited by J. C. Brash, M.A., M.D., F.R.C.S., Professor of Anatomy, University of Edinburgh, and E. B. Jamieson, M.D., Lecturer on Anatomy, University of Edinburgh. Seventh edition. Cloth. Price, $10. Pp. 1,506, with 1,247 illustrations. New York & London: Oxford University Press, 1937.

In thirty-five years this book has gone into the seventh edition. The first three editions, 1902-1909, were prepared under the editorship of D. J. Cunningham, the next three editions under the editorship of Arthur Robinson, and the present edition under the editorship of Drs. J. C. Brash and E. J. Jamieson. The retirement of the previous editor, Professor Robinson, has entailed a change in certain sections of the book, especially Professor Robinson's own chapters on human embryology and the blood vascular and lymphatic systems, which have been revised by Dr. Brash, who has also revised the introduction to the book. This and the retirement of Prof. J. T. Wilson necessitated two new contributors, Prof. R. D. Lockhart of the University of Birmingham, who took over the chapter on myology, and Prof. A. B. Appleton of the University of London, who takes over the chapter on the ductless glands. Since only six years has elapsed since the previous edition was published, substantial changes were necessary in only a few sections. The whole book, however, has been revised and where necessary changed to comply with the present views and methods in the teaching of anatomy. There are many new illustrations. A series of plates has been introduced with photographs of the living body showing the effects of muscles in action, and many roentgenograms illustrating the structure and growth of the skeleton and the position and form of the organs in the body. Also the revision of the Basle Nomina Anatomica, which was approved by the Anatomy Society of Great Britain and Ireland in 1933, has been introduced. The revision in nomenclature is not a sweeping one, however, and much of the apparent change is only a freer translation of the Basle Nomina Anatomica into English than has been used heretofore. A glossary preceding the introduction shows what changes have been made in the nomenclature. T. Wingate Todd, professor of anatomy at Western Reserve University School of Medicine, Cleveland, again has prepared the chapter on the respiratory system and is the only contributor from the United States. The book continues to be well adapted to the needs of both practicing physicians and medical students.

Clinical Electrocardiography. By Sir Thomas Lewis, M.D., F.R.S., D.Sc., Physician in Charge of Department of Clinical Research, University College Hospital, London. Sixth edition. Cloth. Price, 8s. 6d. Pp. 128, with 109 illustrations. London: Shaw & Sons, Ltd., 1937.

The first edition of this popular work—a most welcome pioneer volume it was—appeared in 1913. The present edition shows almost no change from the fifth of seven years ago; there are the same number of pages in this edition as in that of 1930 and in the fourth edition of 1928. One familiar figure, however, on page 6, with the hands and left foot immersed in jars, has been replaced by one showing the more modern and simpler method of attaching the electrodes by means of cuffs. The last four pages, on the electrocardiogram in coronary artery thrombosis, have been rewritten, bringing this subject more nearly to date. It may be of interest to note that the statement at the foot of page 28 concerning the origin of certain anomalous electrocardiograms remains as it was written seven years ago: "Which of these two types represents the human levogram and which the dextrogram has developed into a matter of debate; I therefore leave the curves unidentified with right or left ventricle; and later in this book treat the forms of extrasystole similarly. Actually it is at present a matter of little practical consequence to which ventricle the beats are assigned." Some readers will feel disappointment at the unwillingness of the author to express his opinion on this matter, which has been so much discussed, as also at his omission of any consideration of leads, e. g., lead 4, other than the conventional three leads. This attitude, however, is in line with the plan of the book, which is to avoid topics that Sir Thomas regards as still unsettled or the subject of controversy. In spite of these omissions and of some others that have to do with the more recent developments in electrocardiography, and in spite of the minimal amount of change from the previous edition, the work still remains one of the best guides for the practitioner who desires help in trying to understand the clinical significance of the electrocardiogram. As has been so often remarked, Sir Thomas is a past master in his ability to write clearly and tersely.

Cancer and Diet, with Facts and Observations on Related Subjects. By Frederick L. Hoffman, LL.D., The Biochemical Research Foundation of the Franklin Institute, Philadelphia. Cloth. Price, $5. Pp. 767. Baltimore: Williams & Wilkins Company, 1937.

This book is divided into five parts, not including a group of appendixes. The first part deals with the dietary theories of cancer; as the author says, it is a review of the statements of "more or less competent" authors on the question of the possible dietary or nutritional influence in cancer causation, treatment and control. The second part, which is devoted to the modern diet, deals with the author's hypothesis "that essential errors underlie the modern diet of civilized races, depending chiefly on modified foods from international sources." As a result it is felt that "far reaching changes in bodily functioning and metabolism are introduced which, extending over many years, are among the causes or conditions predisposing to the development of malignant new growths." The third part deals with cancer metabolism, the fourth with dietary facts concerning cancer patients. The fifth contains a general summary and conclusion. Under surgery the index lists only two items, namely, surgical failures and operations ineffective. Nothing is said of x-rays in the index or of roentgenology. Radioactive substances and radium and acid reaction are listed in the index, but only a line or two in the text is devoted to either. The whole book, therefore, is devoted to expanding an argument; namely, that diet is principally responsible for cancer. The book cannot be recommended either as a dispassionate study of diet and cancer or as in any way a well balanced book on cancer. Such volumes do nothing to advance knowledge. By their approach to the subject they actually impede progress by creating a certain amount of support for charlatans who have been exploiting ideas of dietary causation of cancer for many years.

Common Neuroses of Children and Adults. By O. Spurgeon English, M.D., Clinical Professor of Psychiatry, Temple University Medical School, Philadelphia, and Gerald H. J. Pearson, B.A., M.D., Assistant Professor of Pediatrics, Temple University Medical School, Philadelphia. Cloth. Price, $3.50. Pp. 320. New York: W. W. Norton & Company, Inc., 1937.

As stated in the authors' preface, "this book is an attempt to bring together under one cover material which is so voluminous and so widely scattered as to be with difficulty accessible to the student and practitioner of medicine." The authors not only accomplish their purpose but do so in a clear, concise and well organized manner. The freudian concepts of the dynamics of personality formation and the development of personality aberrations are presented in simple language. The neuroses of children and adults with which the physician most commonly deals are described in a systematic fashion. Any practitioner interested in these conditions cannot afford to be ignorant of the psychoanalytic approach to them. To date, and probably for a long time to come, nowhere will he find this information as thoroughly and carefully presented as it is in this book. It must be clearly understood that all the material is presented according to psychoanalytic theories and principles of psychiatry. Any one who is unacquainted with psychoanalytic literature and thought will at first reading find it difficult, if not impossible, to accept much of that which the work includes. For example, in the discussion on some of the phobias, a great deal of gravity is attached to many minor manifestations. As every one knows, fear is an emotional pattern common to the behavior of all children. In most instances the source is not difficult to uncover. The unconscious fear of castration may be a source of fear of animals in isolated cases, but it would seem that a previous experience of a nip on the leg by a too aggressively sadistic puppy is a much more frequent and logical cause. This is not really a defect of the book but an example of psychoanalytic approach with which the average physician will take issue. A criticism that might be offered concerns the dogmatism with which the authors discuss treatments of

the neuroses. According to them, psychoanalysis offers the only solution to most of the problems. Since the book is intended for practitioners and students of medicine, the portions on therapy are rather discouraging. Practitioners of psychoanalysis may find the subject matter somewhat elemental for their purpose, but even they will find much that is of value in the material collected from the recent contributions in the field of child psychiatry. Many orthodox psychiatrists will reject this work because of their refusal to accept psychoanalytic theories; but even the most resistant of these psychiatrists will find in this work much that is new and interesting, if not helpful. The authors have avoided any controversial issues with formal psychiatric technics, except in the last chapter, entitled "Preparation for Psychiatric Work." Herein are set forth the requirements for certification by the American Board of Psychiatry. Following this the authors point out that the important preparation in psychiatry will come "through a knowledge of human psychology and psychopathology which can be acquired only through a study of one's own emotions and their accompanying ideation and behavior and the emotions and resulting ideation and behavior of others."

The Alimentary Factor in Disease. By Max. H. Kuczynski, M.D., D.Sc., Pathologist to the Ministry of Public Health of Peru. Second edition of "Studies on Nutrition." Paper. Price, 3 guilders. Pp. 130. The Hague: G. Naeff, 1937.

This is a curious book and one that is based on a good deal of observation and thinking. The author has worked in many parts of the world on a number of the virus diseases such as encephalitis and yellow fever; also on trypanosomiasis and some of the avitaminoses. Always he has been interested in the fact that the nutrition of an animal and its supply of vitamins influence the type of its reaction to infection. He has found also that the nutrition of an animal can affect its sensibility to roentgen rays. In studying yellow fever he was impressed by the fact that the state of nutrition of the monkeys used as experimental animals had much to do with determining whether or not they survived the infection, and this accounts probably for differences in the mortality rates reported by different investigators. Such differences in nutrition account also for peculiar differences in the reactions of individual animals to inoculation with trypanosomiasis. Kuczynski was interested also in the percentage incidence of gastric ulcers seen in animals given different types of diet and then infected with the virus of encephalitis. In children with poliomyelitis he was impressed with the relation between the amount of physical work done and the incidence of paralysis. The book is hard to review partly because each chapter deals with a different disease and partly because the scores of observations recorded are not always well strung on the thread of the author's thought. The text is at times incomprehensible, perhaps partly because of a poor translation; but with all this the book is thought producing, and every young experimentalist who is starting out to work on animals should look through it and should keep in mind the facts which it brings out.

Une forme cérébrale de la cholestérinose généralisée (type particulier de lipipose à cholestérine). Par Ludo van Bogaert, Hans J. Scherer et Émile Epstein. Paper. Price, 45 francs. Pp. 183, with 61 illustrations. Paris: Masson & Cie, 1937.

This is the most recent monograph on cholesterol lipodosis. In the introduction it is stated that Ludwig Pick and Emil Epstein classify the diseases of lipoid metabolism into three groups which have as a common character deposits of lipids and fatty substances and which have a special characteristic determined lipid. These are the kerasine or cerebroside of Gaucher's disease, the phosphatide of Niemann-Pick's disease, and the cholesterol lipodosis characterized by the presence of cholesterol and its esters. This includes Schüller-Christian's disease. The authors also speak of a fourth group including progressive lipodystrophy, adiposogenital dystrophy and hypophysial obesity. The first chapter is a discussion of the actually known lipodoses. The second discusses the clinical facts of this disorder and the importance of the familial aspect in this entity. The third chapter deals with the anatomic and histopathologic study of the somatic and nervous lesions. The fourth chapter takes up the biochemical and histochemical aspects of the fatty deposits and the final chapter takes up a physiopathologic outline of this disorder. The work is detailed and critically analytic. It has a large bibliography. It should be available to all pathologists, neurologists, internists and pediatricians.

Practical Methods in the Diagnosis and Treatment of Venereal Diseases for Medical Practitioners and Students. By David Lees, D.S.O., M.A., D.P.H. With the following contributors: R. Cranston Low, M.D., F.R.C.P., Consulting Physician for Skin Diseases, Edinburgh Royal Infirmary, William R. Logan, M.D., F.R.C.P., D.P.H., Bacteriologist to Edinburgh Royal Infirmary, and R. C. L. Batchelor, M.A., M.B., F.R.C.S., Director of Department of Venereal Diseases to Edinburgh Royal Infirmary and Edinburgh Corporation. Third edition edited and revised by Robert Lees, M.B., F.R.C.P., Assistant Medical Officer for Venereal Diseases to Edinburgh Royal Infirmary and Edinburgh Corporation. Cloth. Price, $5. Pp. 608, with 93 illustrations. Baltimore: William Wood & Company, 1937.

This publication is in reality a handbook on the clinical management of the venereal diseases prepared for the general practitioner. The third revision is an improvement on the previous excellent work of the late David Lees. That much of the clinical experience on which the book is based was acquired at the Royal Infirmary in Edinburgh is evidenced by the subchapter on gonococcic diseases of the skin, which includes a concise but vivid description of keratoderma blennorrhagica. The schedule of treatment for early syphilis recommended by the Committee of Experts on Syphilis and Cognate Subjects of the Medical Organization of the League of Nations is the scheme of choice of the authors. In the description of regional syphilitic lesions the inexperienced student may be misled by a description of an interesting but rare patient with chancre of the conjunctiva. It is also to be regretted that additional space was not devoted to a more thorough presentation of flocculation tests in the serologic diagnosis of syphilis. The well known preference of British workers for the complement fixation procedure in the serodiagnosis of syphilis probably explains the latter omission. Like most of our British colleagues, the authors have a relatively high regard for the efficiency of complement fixation tests in the diagnosis of gonorrhea. The standards of cure laid down for gonorrhea are interesting and should be a valuable aid to the clinician.

Obstetric and Gynecologic Nursing. By Frederick H. Falls, M.S., M.D., F.A.C.S., Professor of Obstetrics and Gynecology, University of Illinois College of Medicine, and Jane R. McLaughlin, B.A., R.N., Supervisor of the Department of Obstetrics and Gynecology, Research and Educational Hospital, University of Illinois College of Medicine. Cloth. Price, $3. Pp. 492, with 83 illustrations by Charlotte S. Holt. St. Louis: C. V. Mosby Company, 1937.

In line with the trend in medical education in this country, the authors have combined the subjects of obstetrics and gynecology in one book. Also in accordance with present custom in the preparation of books for nurses, this book represents the combined effort of a physician and a nurse, both of whom are leaders in their field. The book is well written and its thirty-four chapters contain the essential facts which nurses should know about obstetrics and gynecology. The value of the book is greatly enhanced by the illustrations (one is repeated), which are highly instructive. Even though the book does not contain as much information as some other books on obstetrics for nurses, it will nevertheless admirably serve the purpose for which it was written.

Curieterapia in dermatologia. Parte generale: Principi fondamentali della curieterapia. Le trasformazioni radioattive. Basi biologiche. Azione delle varie irradiazioni sulla pelle. (Alfa, Beta, Gammaterapia). Parte speciale: Technica curieterapica nelle varie dermatosi. Dal Prof. Vincenzo Palumbo, direttore Istituto radioterapico italiano. Cloth. Price, 36 lire. Pp. 87, with 76 illustrations. Belluno: Casa editrice libraria A. Salvador, 1937.

In this little volume Palumbo discusses the value of radium in the treatment of diseases of the skin. The general part of the book takes up the physical foundations of radium therapy, the radioactive transformations, the biologic basis of radium therapy and the action of alpha, beta and gamma radiation on the skin. In the special portion of the book the technical aspects of the radium treatment of various dermatoses is illustrated. The excellence of the results that may be obtained by correct treatment is shown by many photographs of patients. In no sense can this book be regarded as an exhaustive treatise; rather it constitutes a brief setting forth of well established facts.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Optometry Practice Acts: Federal Court May Not Enjoin Enforcement of Injunction Issued by State Court.—The superior court, Mecklenburg County, N. C., enjoined Benjamin Ritholz and others, doing business as the National Optical Stores Company, from practicing optometry in North Carolina or from furnishing any kind of material or apparatus for ophthalmic use without a written prescription from a person, other than an employee of the defendants, licensed to practice optometry or medicine in North Carolina. Ritholz and the other defendants in the superior court then instituted an action in the federal district court, middle district, North Carolina, against the state board of examiners in optometry, the governor, the attorney general, and the sheriff of Mecklenburg County, to restrain the enforcement against Ritholz and the others of (1) the provisions of the North Carolina optometry act and (2) the terms of the injunction issued by the superior court.

The National Optical Stores Company, according to the court, was engaged in the manufacture of eyeglasses, lenses and frames in the city of Chicago. It possessed no license to practice either optometry or medicine in North Carolina. The superior court found that Benjamin D. Ritholz, Samuel J. Ritholz, Morris I. Ritholz, Fannie Ritholz, Sylvia Ritholz and Sophia Ritholz, trading as the National Optical Stores Company, had offices in Charlotte, N. C., and that they employed in those offices one Dr. L. H. Coffey, at a salary of $45 a week; that the defendants, through their agents, advertised in newspapers and by radio that they would sell complete glasses for $3.45 and guaranteed satisfaction; that a large number of persons who made affidavits responded to these advertisements by going to the offices of the defendants, but none of them were able to purchase glasses for the sum stated but on the contrary most were required to pay several times that amount; that several of the persons who furnished affidavits found their glasses completely unsatisfactory and in some instances the glasses were, according to the affidavit of a doctor of medicine who specialized in the treatment of the eyes, positively injurious to the eyesight of the persons who had purchased them. The superior court further found that the examination of the eyes of persons who purchased glasses from the defendants was made for the most part by Dr. L. H. Coffey, who was licensed to practice medicine in North Carolina, but that in some instances he had been assisted in making the examination of eyes by persons licensed neither as optometrists nor as doctors of medicine. No separate charge was made for such examinations, but the glasses were sold for a price which included the examination of the eyes. The examinations were made by Dr. Coffey by the use of a trial frame into which glasses were fitted and no other instrument of any kind was used by Dr. Coffey. When glasses were sold, apparently the prescriptions were sent to the offices in Chicago and the glasses sent from there to the North Carolina office. The superior court also found as a fact that one G. P. Sayers, another employee of the National Optical Stores Company in its North Carolina offices, sold or attempted to sell, furnish, replace or duplicate lenses, frames and mountings, and replaced them by ordering them from the Chicago office, without a written prescription from persons authorized under the laws of North Carolina to practice optometry or medicine and that this constituted the practice of optometry by the company.

In this case, said the federal district court, the state court held that the method of doing business which Ritholz and the others pursued in North Carolina constituted a violation of the optometry practice act and enjoined them from continuing to do business in that way. Ritholz and the others now seek, the court continued, to protect the method of doing business by enjoining any interference with that business by an enforcement of the optometry practice act. But, said the court, since no effort was being made to enforce the act against them except through the proceedings in the state court, the present action constituted an attempt to enjoin the enforcement of the decree of the state court. A writ of injunction, however, cannot be granted by any court of the United States to stay proceedings in any court of a state, except cases in which such injunction may be authorized by any law relating to proceedings in bankruptcy. 28 U. S. C. A., sec. 379. Irrespective of the provision in the judicial code just cited, the court said, the present suit must be dismissed as an attempt to review by a bill in equity in a federal court the decision of a state court. The issue involved, both in the case decided by the state court and in the case in the federal court, was the right of Ritholz and the others to do business under the methods they were pursuing. This issue was squarely determined against them in the suit in the state court and an injunction was issued accordingly. The rule is well settled that one court of equity will not enjoin proceedings in another court of coordinate jurisdiction. The remedy of the plaintiffs, the court pointed out, if they are aggrieved by the action of the state court, is to appeal to the state supreme court, the action of which in proper cases may be reviewed by the Supreme Court of the United States by writ of certiorari. After litigating the issue in the state court, however, they cannot remove the case to the federal district court, nor can they obtain a review of an adverse decision by filing a bill in equity in the federal district court.

For the reasons stated, the federal district court dismissed the plaintiffs' bill.—*Ritholz et al. v. North Carolina State Board of Examiners in Optometry et al., 18 F. Supp. 409.*

Medical Practice Acts: Violation of Harrison Narcotic Act Involves Moral Turpitude.—The medical practice act of Arizona authorizes the board of medical examiners to revoke the license of a physician who is guilty of unprofessional conduct and defines that term to mean, among other things, the conviction of any offense involving moral turpitude. The board revoked Du Vall's license to practice medicine. The superior court of Maricopa County, in a certiorari proceeding, affirmed the order of the board, and Du Vall appealed to the Supreme Court of Arizona.

The extent of the power of the court, said the Supreme Court, to review on certiorari is limited to a determination of the question as to whether the inferior tribunal regularly pursued its authority. If the facts stated in the complaint against Du Vall were sufficient to confer jurisdiction on the board to proceed to a hearing, and if a hearing was had at which he was given an opportunity to present his defense, errors and irregularities in the proceedings and in the board's conclusion may not be reviewed on certiorari. While the complaint should state a statutory ground or grounds as cause for revoking a license, it is not necessary that such ground or grounds be set forth with the preciseness and particularity observed in an indictment or information or in a complaint in a civil action. The proceedings before the board are more or less informal. If the accusation is sufficient to advise the physician of the nature and character of the charges so that he may prepare himself to defend thereon, it is sufficient.

The first count of the complaint charged that Du Vall "dispensed, prescribed by prescription or sold drugs for other than medical purposes to a person who was an habitual user of such drugs without any intent or purpose to cure said habitual user of the use of said drugs" and that such conduct was contrary to the ethics and professional conduct of a physician. Du Vall contended that this count was insufficient both in fact and in law, that the statutory definition of "unprofessional conduct" was exclusive and that what he was charged with doing in the count did not fall within such definition. He contended also that, if what was charged in the count be admitted as true, it would not constitute unprofessional or unethical conduct, because it was not charged that the drugs dispensed, prescribed or sold were of the habit-forming kind, such as morphine or cocaine, or that such drugs were destructive to health or character. With this last contention the court agreed and consequently held that the count should be rejected as not being sufficient either in law or in fact. The court deemed it unnecessary to decide whether the statutory definition of "unprofessional conduct" was or was not exclusive.

The second count in the complaint charged that Du Vall had been convicted under an indictment charging him with violating the Harrison Narcotic Act and that the offense for which he was convicted was one involving moral turpitude. The

question here presented, the court said, is: Does the conviction of a regular physician under the Harrison Narcotic Act involve moral turpitude? Just what crimes involve moral turpitude is not always easy to say. Generally speaking, crimes that are malum in se, which are wrong in themselves, involve moral turpitude, while those that are malum prohibitum, acts that are not wrong in themselves but are crimes because prohibited by law, do not. This distinction is not always true. Assault and battery, for instance, is malum in se but rarely involves moral turpitude. One of the great evils of the day, the court pointed out, is the consumption of narcotic drugs. Because so many persons become addicts, most of the states, if not all of them, have enacted laws restricting the right to dispense or prescribe such drugs. While the United States cannot control the use of narcotic drugs, it has under the taxing power made the traffic in them more difficult. If there is any one who is to be pitied, the court said, it is the addict of habit-forming drugs of the narcotic kind. He is usually a hopeless loss to society. He is a real menace. He will do most anything to secure the drug to satisfy his cravings and under its influence commit most desperate crimes. No no knows this better than the members of the medical profession, bound by their honor and the Hippocratic Oath to the highest ideals in their relation to society and especially those seeking their advice and help. When one of these has been convicted of violating the Harrison Narcotic Act, the court said, he is guilty of "an act of baseness . . . contrary to the accepted and customary rule of right and duty between man and man." In the present case, the indictment on which Du Vall was tried charged him with making, on the same day, two separate sales to an addict, one for four grains of morphine and the other for three, not in the course of his professional practice and not in pursuance of a written order. How could it be said, the court questioned, that a physician who would do what is charged here is of good moral character, or that he is not prostituting his high profession for material gain?

After referring to several definitions of the term "moral turpitude," the court said that it seemed reasonable that the Arizona legislature, when it provided that a physician's license should be revoked when he was convicted of a crime involving moral turpitude, must have meant as measured by the standards of policy and morality as found in Arizona laws. At the time Du Vall was charged with having violated the Harrison Narcotic Act, the same act under the Arizona law was a felony, punishable by a fine of not less than fifty nor more than one thousand dollars or by confinement in the penitentiary for not more than five years, or both. "So we must say that those things which are discountenanced and regarded as evil and accordingly forbidden by society are immoral and that the doing of them contrary to the sentiment of society thus expressed involves moral turpitude, and this regardless of the punishment imposed for their doing." *State* v. *Malusky*, 59 N. D. 501, 230 N. W. 735, 71 A. L. R. 190. The proceeding before the medical board to revoke a license is not criminal, the court said, and does not require that every doubt, as in a criminal case, be resolved in favor of the innocence of the licensee. A conviction under the Harrison Narcotic Act negatives all presumptions of good faith on the part of the defendant and brands him as a person of bad moral character, unfit to practice medicine.

Du Vall finally contended that the order revoking his license was void because it failed to "show the facts essential to the jurisdiction of the board making it." The order of the board, omitting formal parts, provided:

> The said Board having fully considered the evidence here to for [sic] submitted, and being fully advised in the premesises [sic] find [sic] as follows:
>
> "That the said respondent Dr. Claude Emerson DuVoll [sic] has been found guilty of unprofessional conduct, therefore the Board by unanimous [sic] vote here by [sic] revokes the license of the said respondent Dr. Claude Emerson DuVoll [sic].

In support of his contention Du Vall cited *Blunt* v. *Shepardson*, 286 Ill. 84, 121 N. E. 263, in which case the entire proceeding was in parol and the order of revocation gave no reason for the revocation. The court very properly held the proceeding void. What was done in that case, however, was very different from the situation here, the court said. Du Vall was formally charged with unprofessional conduct and one of the charges was incontrovertibly proved. He was given a formal hearing and found guilty of unprofessional conduct. While the order does not state the particular cause for the revocation of his license, reference to the record makes it very definite that it was based on his conviction of a crime involving moral turpitude.

The Supreme Court, therefore, affirmed the judgment of the superior court upholding the revocation of Du Vall's license.—*Du Vall v. Board of Medical Examiners of Arizona (Ariz.), 66 P. (2d) 1026.*

Pharmacists: Liability for Mistake in Filling a Prescription.—A physician, called to treat the plaintiff for a minor ailment, gave him a written prescription which read "Tabletae hydrargyri chloridi mitis comp., .·. . Two at bed time as directed," and orally directed that the medicine be taken internally. The prescription was sent to a pharmacy owned by the defendants. The pharmacist, one of the defendants, in filling the prescription, dispensed bichloride of mercury tablets of 7½ grains each instead of the compound cathartic tablets called for by the prescription. On each of the tablets dispensed appeared the word "poison" and a skull and cross-bones. Attached to the container was the regular label of the pharmacy on which appeared the printed words "for external use only," and the typewritten instructions "two at bed time, as directed." The word "poison" in large heavy lettering and a skull and cross-bones were not printed on the label, as was required by law, to designate the poisonous character of the contents of the container. The plaintiff became violently ill after taking two of the tablets. His illness, however, did not prove fatal. He later sued the defendants to recover damages for the suffering and disability which he claimed was the result of their error. From a judgment in favor of the plaintiff for $350, both parties appealed to the court of appeal of Louisiana, Orleans.

The defendants contended that inasmuch as customarily bichloride of mercury is compounded in tablets and compound cathartic in pills, the pharmacist was justified in filling the prescription as she did because the use of the word "tabletae" in the written prescription indicated that the physician intended to prescribe bichloride of mercury. This contention, however, did not meet with the court's approval because, the court said, the words used in the prescription clearly meant compound cathartic and not bichloride of mercury. Even if there was justification for the error, there was extreme negligence in delivering this deadly poison in a container which did not on its face show the dangerous character of the contents as was required by law. The plaintiff was not negligent, as the defendants contended, in failing to notice the small and insignificant warnings on the tablets, consisting of the word "poison" and a skull and cross-bones. Neither was he negligent in failing to notice that the container bore the printed prescription "for external use only," or if he did notice it, in assuming the oral and typewritten instructions of the physician should be followed instead of the printed directions on the container. The typewritten inscription "two at bed time, as directed," said the court, would ordinarily be taken to mean that the medicine should be taken internally.

Although the court was of the opinion that the plaintiff was entitled to a judgment, it could not agree with the plaintiff's contention that the judgment was insufficient. The evidence showed that the plaintiff had been suffering with other diseases and that much of his disability and pain resulted from them and not from the pharmacist's mistake. The court concluded, therefore, that the judgment for $350 amply compensated the plaintiff for his sufferings which had resulted from the pharmacist's error.

Accordingly, the court of appeal affirmed the judgment in favor of the plaintiff.—*Marigny v. Dejoie et al. (La.), 172 So. 808.*

Society Proceedings

COMING MEETINGS

American Academy of Orthopedic Surgeons, Los Angeles, Jan. 16-20. Dr. Carl E. Badgley, 1313 East Ann St., Ann Arbor, Mich., Secretary.

Society of American Bacteriologists, Washington, D. C., Dec. 28-30. Dr. I. L. Baldwin, College of Agriculture, University of Wisconsin, Madison, Wis., Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers in continental United States and Canada for a period of three days. Periodicals are available from 1927 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American J. Digest. Dis. & Nutrition, Fort Wayne

4: 487-544 (Oct.) 1937

*Artificial Fever in Treatment of Ulcerative Colitis: Preliminary Report. L. K. Ferguson, F. Fetter and T. G. Schnabel, Philadelphia.—p. 487.

Studies in Intermittent Heat Sweats: Chlorides and Acid-Base Balance. L. L. Hardt and Alice Palmer, Chicago.—p. 489.

Food Habits of the Patient with Peptic Ulcer. Margaret Elder and E. S. Emery Jr., Boston.—p. 493.

Treatment of Peptic Ulcer by Diet of Goldberger and Wheeler. H. A. Warren, D. G. Friend and E. S. Emery Jr., Boston.—p. 495.

Dental Caries and Paradental Disturbances: III. Dietary History and Its Value in Dental and Medical Practice. Nina Simmonds, San Francisco.—p. 497.

Syphilis of the Stomach. H. J. Mayer, Los Angeles.—p. 503.

Carcinoma of the Small Intestine as a Hidden Cause of Anemia. A. R. Hatcher and K. E. Voldeng, Wellington, Kan.—p. 507.

Errors in Gastro-Enterologic Diagnosis. M. Golob, New York.—p. 512.

Tumors of Small Intestine: Review of Literature and Report of Eight Additional Cases. J. J. Stein, Hines, Ill.—p. 517.

The Mechanism of Milk Clotting: II. Role of Hydrogen Ion Concentration. I. N. Kugelmass, New York.—p. 523.

Artificial Fever in Treatment of Ulcerative Colitis.—Ferguson and his associates treated five cases of ulcerative colitis by artificial fever, for the production of which they used the Kettering hypertherm. Their method of treatment consisted of two and one-half to three hours of fever between 104 and 105 F. (rectal) three times a week. The number of treatments varied between seven and seventeen, the average being twelve per patient. Each patient responded favorably to fever therapy, the clinical improvement preceded the improvement in the proctoscopic appearance. In most cases, after three or four treatments the number of stools was markedly reduced and bleeding and tenesmus were less. The patients' appetites improved and their weights began to increase. In spite of the clinical improvement, fever treatments were continued until the proctoscopic appearance also had improved, except in one patient, who refused to have more than seven fever treatments. In this patient the appearance of the intestine on proctoscopic examination continued to improve, in spite of the fact that fever treatments were not continued. The use of artificial fever in the treatment of ulcerative colitis is not regarded as a treatment that will produce a permanent cure.

American Journal of Tropical Medicine, Baltimore

17: 639-772 (Sept.) 1937

Spotted Fever in Tobia, Colombia: Preliminary Report. L. Patino, A. Afanador and J. H. Paul, Bogotá, Colombia.—p. 639.

Present Day Methods for Study and Control of Yellow Fever. F. L. Soper, Rio de Janeiro, Brazil.—p. 655.

*Epidemic of Urban Yellow Fever Which Originated from a Case Contracted in the Jungle. A. M. Walcott, Rio de Janeiro, Brazil; E. Cruz, A. Paoliello and J. Serafim Jr.—p. 677.

Variations in Gametocyte Production in Avian Malaria. Winton Elizabeth Gambrell, Chicago.—p. 689.

Comparative Effects of Blood of Different Species of Vertebrates on Egg Production of Aedes Aegypti Linneaus. P. A. Woke, Baltimore.—p. 729.

Granuloma Inguinale. R. D'Aunoy and E. von Haam, New Orleans.—p. 747.

The Sting of an Ant. N. A. Weber, Grand Forks, N. D.—p. 765.

Epidemic of Urban Yellow Fever.—Walcott and his colleagues present data from which it seems probable that a small epidemic of yellow fever originated through a person who became infected in the jungle but later remained during almost the entire period of his attack in the town of Cambará, where he infected the Aedes aegypti mosquitoes, which in turn caused the outbreak of the urban yellow fever. It is not possible to deny absolutely that the epidemic may have been initiated by some unrecognized case of urban yellow fever in a person arriving from another city or town, but persistent inquiries failed to disclose acceptable evidence for such a conclusion. The first three cases occurred in close neighbors on the same small premises, and the epidemic developed among persons living in nearby houses who had not been absent from Cambará for three weeks previously. The outbreak subsided promptly following the introduction of adequate measures for the prevention of the propagation of Aedes aegypti mosquitoes.

Annals of Surgery, Philadelphia

106: 801-960 (Nov.) 1937

Early and Remote Effects of Total and Partial Paravertebral Sympathectomy on Blood Pressure: Experimental Study. K. S. Grimson, H. Wilson and D. B. Phemister, Chicago.—p. 801.

Studies on Etiology of Renal Hypertension. A. Blalock and S. E. Levy, Nashville, Tenn.—p. 826.

Production of Hypertension by Constricting the Artery of Single Transplanted Kidney: Experimental Investigation. F. Glenn, C. G. Child and G. J. Heuer, New York.—p. 848.

Epinephrine Hypertension: Effect of Continuous Intravenous Injection of Epinephrine on Blood Pressure: Experimental Investigation. J. Van Prohaska, H. P. Harms and L. R. Dragstedt, Chicago.—p. 857.

*Postoperative Thrombosis and Embolism. F. W. Bancroft, Margaret Stanley-Brown and E. Chargaff, New York.—p. 868.

Treatment of Embolism of Greater Arteries. C. C. Lund, Boston.—p. 880.

*Studies in Etiology of Acute Appendicitis: Significance of Structure and Function of Vermiform Appendix in Genesis of Appendicitis: Preliminary Report. O. H. Wangensteen, R. E. Buirge, C. Dennis and W. P. Ritchie, Minneapolis.—p. 910.

Repair of Peripheral Nerve Injuries. M. B. Tinker and M. B. Tinker Jr., Ithaca, N. Y.—p. 943.

Postoperative Thrombosis and Embolism.—Bancroft and his co-workers are confident that the physical factors accepted by most authors (dehydration, stasis, infection and trauma) are the main causes of postoperative thrombosis, thrombophlebitis and embolism. In addition to these factors, it is felt that there must be a biochemical change in the blood which precedes and accompanies thrombophlebitis and embolism, because all the physical factors may be present in certain patients and no accident may occur, while in other patients the minimal number of the physical factors may be present and an accident may result. It is recognized that there are definite bleeding diatheses. If, therefore, it is true that there are potential bleeders, one can readily assume that there are potential clotters. If this theory is true, the authors believed that a careful analysis of the blood factors involved in clotting would reveal a significant change before a thrombus occurs. They describe the tests for blood clotting factors, give the result of their prophylactic therapeutic program and discuss the factors entering into blood clotting; viz., fibrinogen, calcium, prothrombin and thromboplastin. The blood of 920 persons was examined. Of these, 111, or 12 per cent, showed high clotting indexes. Only 46 per cent of the patients having high indexes received prophylactic treatment. No accident occurred in the treated cases. In the untreated group nine accidents occurred. Two of these were unrecognized, as the fibrinogen was the only high factor. Newer preparations of heparin for prophylaxis are much more stable than those previously presented by manufacturing chemists. In the authors' early studies they found that heparin injected intravenously lowered the clotting factors in the blood for only an hour or two and then the blood regained its normal tendency. In the present method of injecting into the muscles about the operative site, the heparin is absorbed much more slowly and therefore must have a longer period of potency. Epinephrine should be added to the mixture so that the possibility of hemorrhage is obviated. In only 1 or 2 per cent of all postoperative cases does thrombosis and embolism develop. The clotting factors are a fairly accurate index of a patient's clotting tendencies and, if these patients are observed early and placed on a bleeding diet and given sodium thiosulfate, the morbidity may be definitely reduced.

Etiology of Acute Appendicitis.—In the light of the knowledge that the vermiform appendix of man secretes fluid, Wangensteen and his colleagues state that its behavior under conditions of obstruction becomes understandable. Whereas it may have been more readily believed that this segment of the intestinal canal, so intimately related to the colon, should be identified with absorption, the demonstration of its secretory function, even though it is slight, lends trustworthy credibility to an obstructive origin of appendicitis. That the vermiform

appendix of man may become easily obstructed is obvious. How this obstruction may come about is not so readily discernible. How the appendix may become totally obstructed in other manners than by foreign bodies and appendicoliths demands explanation. That swelling of the mucous and submucous lymphoid tissue may bring about obstruction of the lumen appears reasonable; that augmentation of the normal physiologic obstruction to emptying by reflex nervous causes may initiate circulatory damage to the appendical mucosa and set in motion the effects of continued luminal obstruction would seem to be not unlikely. Observations suggest that the mechanism for production of fluid by the appendix becomes less efficient with increase in age, when appendicitis is also less commonly observed. A closed loop in which secretion occurs would appear to be particularly hazardous when the luminal capacity is small, as it is in the vermiform appendix. Burget and Dragstedt and their associates have indicated how temporary aspiration of a closed loop, or preliminary washing of it, may permit of its being tolerated with the avoidance of rupture. Undoubtedly the same holds true of the vermiform appendix. With gradual development of obstruction or obliteration, undoubtedly complete luminal obstruction may be withstood without rupture.

Archives of Dermatology and Syphilology, Chicago

36: 937-1128 (Nov.) 1937

Cutaneous Tuberculosis in the Negro: A Clinical Entity: Report of Two Cases (One Associated with Syphilis). D. Bloom and H. V. Mendelsohn, New York.—p. 937.

Lesions of Skin and Subcutaneous Tissue in Diseases of Peripheral Circulation. E. D. Telford, Flintshire, England.—p. 952.

Sensitivity to Both Trivalent and Pentavalent Arsenicals. E. Epstein, Oakland, Calif.—p. 964.

Experimental Arsphenamine Dermatitis: Observations on Its Allergic Nature, with Especial Attention to Schultz-Dale Phenomenon. F. E. Cormia, Montreal.—p. 970.

*Pyogenic Relapse and Sensitiveness to Light in Certain Dermatoses: Influence of Factor of Intercurrent Infection. J. H. Stokes, Philadelphia, and J. L. Callaway, Durham, N. C.—p. 976.

Ringworm Fungus Growing as a Saprophyte Under Natural Conditions. I. Muende and P. Webb, London, England.—p. 987.

Pityriasis Varioliformis Acuta: Report of Case of Extensive Involvement Associated with Bullae. S. S. Robinson, Los Angeles.—p. 991.

Dermal Reticulosis of Obscure Nature: Report of Case. A. N. Goyle, A. Vasudevan and K. G. Krishnaswamy, Madras, India.—p. 998.

Oligosepsis. L. I. Hallay, Middlesboro, Ky.—p. 1008.

Penoscrotal Elephantiasis of Lymphogranulomatous Origin: Description of Case with Psoriasiform Cutaneous Lesions and Others Resembling an Ecthymatous Pyoderma. W. E. Coutts and H. Ahumada, Santiago, Chile.—p. 1014.

Rhinoscleroma: Report of Case. H. E. Alderson, San Francisco.—p. 1018.

Demonstration of Pemphigus Toxin in Fresh and in Dry Blood. D. I. Macht, Baltimore.—p. 1022.

*Effect of Oils Containing Unsaturated Fatty Acids on Patients with Dermatitis: Brief Report of an Experimental Study in Guinea Pigs. J. E. Ginsberg and C. Bernstein Jr., with technical assistance of L. Vivian Iob, Chicago.—p. 1033.

Kline Exclusion Test in Prevention of Transfusion Syphilis. R. Straus, Cleveland.—p. 1039.

Keratosis Blennorrhagica with Corneal Lesions: Further Observations on Therapeutic Effect of Hyperpyrexia. E. Epstein, Oakland, Calif., and S. O. Chambers, Los Angeles.—p. 1044.

Scleredema Adultorum (Buschke): Report of Case Involving the Tongue. L. J. Frank, Sioux City, Iowa.—p. 1052.

Scleroderma and Sclerodactylia Associated with Intermittent Claudication. S. S. Robinson, Los Angeles.—p. 1054.

Ainhum: Report of Six Cases in New York. M. T. Horwitz, Philadelphia, and I. Tunick, New York.—p. 1058.

Boric Acid-Starch Poultice. D. W. Montgomery, San Francisco.—p. 1064.

Ectodermosis Erosiva Pluriorificialis: Its Resemblance to Human Form of Foot and Mouth Disease and Its Relation to Erythema Exsudativum Multiforme. J. V. Klauder, Philadelphia.—p. 1067.

Effect of Inflammation of Skin on Urinary Excretion of Ketones. T. Cornbleet and R. I. Klein, Chicago.—p. 1078.

Dermatitis Due to Japanese Lacquer: Report of Case of Involvement of Fifteen Years' Duration. L. Hollander and J. M. Shelton, Pittsburgh.—p. 1081.

Sensitiveness to Light in Certain Dermatoses.—For some time Stokes and Callaway have suspected that intercurrent infections, especially in epidemic waves, exercise a sensitizing influence in dermatoses with an underlying allergic or infectious-allergic complex. In the past year in their practice this role has been assumed, apparently, by an "influenzal" type of naso-respiratory, gastro-intestinal and general infection the epidemic character of which is attested by a number of official reports and such analyses as that of Gover, which indicated an epidemic prevalence approaching twenty times the normal expectancy in one of eleven outbreaks. It appears from a study of the incidence of pustular relapses and pyogenic dermatoses in their typical dermatologic practice in comparison with that of regionally epidemic infections of the respiratory and gastro-intestinal tracts that intercurrent infections, in part at least presumably of the virus type, predispose definitely to relapse and presumably to clinically pyogenic and partly pyogenic (acneform) eruptions. Such relapses show a tendency to occur in persons with familial or hereditary predisposition to pyogenic attacks, occur after mild as well as severe attacks of the intercurrent infection and may even be suspected of occurring in comparatively asymptomatic carriers, surrounded by patients with symptomatically active disease. Their onset tends to follow a period of incubation of from seven to eleven days, suggesting the development of an allergic or hypersensitive state; the development of such a state as part of an infectious-allergic complex is still further suggested in certain cases of relapse of primary pyogenic infection by the appearance of sensitiveness to light and apparently also of sensitiveness to both light and drugs.

Fatty Acids and Dermatitis.—Ginsberg and Bernstein made repeated studies of the blood lipids on fifty-six subjects with chronic dermatitis to determine the effect of ingestion of oils (linseed, corn or cod liver) containing unsaturated fatty acids. Their observations give them no reason to believe that there was any characteristic abnormality of the blood lipids in the patients whom they treated or that any specific benefit arises from feeding such patients oils containing highly unsaturated fatty acids. Prolonged administration of unsaturated oils to guinea pigs which had been sensitized to horse serum did not prevent anaphylaxis following injection of horse serum.

Archives of Otolaryngology, Chicago

26: 387-508 (Oct.) 1937

Hearing Before and After Radical Mastoidectomy: Plea for Avoidance of This Operation by Early Adequate Drainage; Summary of Fifty-Four Cases with Audiograms and Clinical and Roentgen Findings. E. P. Fowler, New York.—p. 387.

Solitary Xanthoma of External Auditory Canal. H. C. Rosenberger, Cleveland.—p. 395.

Characteristics of Modern Electrically Operated Audiometers: Qualitative and Quantitative Analysis. M. S. Ersner, L. Podolsky and D. Myers, Philadelphia.—p. 400.

Pneumothorax Complicating Tracheotomy in Fulminating Laryngotracheobronchitis: Report of Case. W. L. Simpson, Memphis, Tenn.—p. 411.

Vegetable Foreign Body Encapsulated in a Vocal Cord: Report of an Unusual Case. R. S. Rosedale and H. E. Bozer, Buffalo.—p. 415.

*Role of Helium in Cases of Obstructive Lesions in Trachea and Larynx. J. D. Kernan and A. L. Barach, New York.—p. 419.

Cristectomy: Permanent Window in Antrum for Chronic Maxillary Sinusitis. J. H. Childrey, San Francisco.—p. 448.

Myxoma of Palate and Pharynx: Report of Case. J. A. Babbitt and D. B. Pfeiffer, Philadelphia.—p. 453.

Acute and Chronic Purulent Otitis Media, Sinus Thrombosis and Suppuration of Petrous Pyramid. S. J. Kopetzky, New York.—p. 460.

Helium in Obstructive Lesions in Trachea.—In the treatment of twenty-one patients with obstruction in some part of the pulmonary airway, Kernan and Barach employed the inhalation of a mixture of helium and oxygen. Of these patients, eleven received marked relief from the signs of obstructed dyspnea. In seven of these there was need for tracheotomy, although one of them had tracheotomy as a precautionary measure two days later. All of them recovered. Although the remaining four patients experienced marked relief as a result of the helium and oxygen therapy there was ultimately a fatal outcome, as a result of tumor in two, of a thyroid crisis in one and of bronchopneumonia following recovery and subsequent tracheotomy in one. In three cases little or no relief was evident and in the remaining seven cases partial or temporary relief was obtained; in three cases in which tracheotomy was ultimately performed recovery took place and the other four patients were fatally ill, one with compression due to a mediastinal tumor, one with compression due to aneurysm and two with bronchopneumonia. Observation of the patients who received positive pressure in addition to helium and oxygen therapy led to the belief that pressure would have been an additional help in many of the other cases. In some instances helium and oxygen therapy is entirely palliative. When the obstruction is due to pressure of a neoplasm below the site for tracheotomy, the only alternative to treatment with a mixture of helium and oxygen is death by strangulation. In one instance the treatment could be continued until roentgen therapy accomplished removal of the

constricting force. If prolongation of life is itself justifiable through the use of roentgen therapy, helium and oxygen therapy, in order to sustain life until an attempt may be made to reduce a tumor by x-rays, is indicated. When the pressure is due to an advancing aneurysm, for which there is no medical therapy, it seems pointless to use helium and oxygen therapy and precipitate a situation which would necessitate indefinite treatment. The most favorable field for this treatment appears to be the inflammatory swellings in the air passages that are due to infection or to mechanical irritation. If the patient can be tided over a certain period without suffocation by inhaling helium and oxygen under a slight pressure, the subsidence of the infection or the traumatic inflammation makes complete recovery possible. The authors' intention is not to minimize the importance of tracheotomy but to emphasize that the ability to dispense with tracheotomy by employing helium and oxygen therapy makes less likely the complications following tracheotomy, such as descending infection and bronchopneumonia. In other cases, those in which tracheotomy is indicated, a period of relative relief by the inhalation of helium and oxygen makes the operation less dangerous.

California and Western Medicine, San Francisco

47: 217-288 (Oct.) 1937

Anesthetic Gas Mixtures: Their Explosion Hazards. C. G. Toland and W. P. Kroger, Los Angeles.—p. 223.
Pituitary Dwarfs: Their Growth and Treatment: Observations on Twelve Cases for Periods of One to Eight Years. Leona M. Bayer and H. Gray, San Francisco.—p. 228.
Intrapartum and Postpartum Hemorrhage. C. A. DePuy, Oakland.—p. 233.
Simple Eye Tests in a Pediatrician's Office: Their Value. Helen M. Johnson and W. P. Lucas, San Francisco.—p. 236.
Maternal and Child Welfare: Its Progress Under the Social Security Act: Relation of the Act to Obstetrics in California. L. G. McNeile, Los Angeles.—p. 240.
Branchiogenetic Cysts. E. Larson, Los Angeles.—p. 244.

Colorado Medicine, Denver

34: 697-768 (Oct.) 1937

The Health Officer's New "Problem Child." R. R. Spencer, Washington, D. C.—p. 716.
Recent Advances in Radiation Therapy. P. R. Weeks, Denver.—p. 722.
Care of the Ear in Acute Otitis Media. F. L. Beck, Cheyenne, Wyo.—p. 734.

Iowa State Medical Society Journal, Des Moines

27: 511-560 (Oct.) 1937

Medical Economics. C. G. Heyd, New York.—p. 511.
Surgical and Hormone Treatment of Undescended Testicle. J. W. Duncan, Omaha.—p. 514.
Advantages of Biomicroscopy in Certain Cases of Beginning Ocular Pathology. W. H. Maloy, Shenandoah.—p. 517.
Advantages and Disadvantages of Some New Procedures in Cataract Surgery. E. P. Weih, Clinton.—p. 520.
Osteogenic Sarcoma. J. T. Hanna, Burlington.—p. 524.
Vincent's Infection in Children. R. Stahr, Fort Dodge.—p. 529.
A Discussion of Obesity. M. C. Wheelock, Mount Pleasant.—p. 530.

Journal of Immunology, Baltimore

33: 251-336 (Oct.) 1937

Further Experiments on Inactivation of Herpes Virus by Vitamin C (*l*-Ascorbic Acid). Margaret Holden and Eleanora Molloy, New York.—p. 251.
Passive Anaphylactic Sensitivity to Pneumococcic Capsular Polysaccharides. K. Goodner and F. L. Horsfall Jr., New York.—p. 259.
Serologic Specificity in Pyridine Derivatives. K. Landsteiner and N. W. Pirie, New York.—p. 265.
Antilymphocytic Serum. W. B. Chew and J. S. Lawrence, Rochester, N. Y.—p. 271.
Type-Specific Antipneumococcus Rabbit Serum for Therapeutic Purposes: Production, Processing and Standardization. K. Goodner, F. L. Horsfall Jr. and R. J. Dubos, New York.—p. 279.
Inhibition of Complementary Activity by Anticoagulants. A. Wadsworth, F. Maltaner and Elizabeth Maltaner, Albany, N. Y.—p. 297.
Heterogenetic Hemagglutinins in Man Following Therapeutic Injections of Immune Serums Produced in Rabbits. F. Schiff, New York.—p. 305.
Flocculation of Alcoholic Red Cell Extracts by Different Types of Human Heterogenetic Hemagglutinins. F. Schiff, New York.—p. 315.
*Antitoxic Response to Diphtheric Antigens in Children. D. T. Fraser and K. C. Halpern, Toronto.—p. 323.

Antitoxic Response to Diphtheric Antigens in Children.—Fraser and Halpern give the results of approximately 600 titrations of serums from 244 children, given three injections of "unmodified" diphtheric toxoid, by showing the percentage distribution of children, by antitoxin levels, at certain intervals of time after the last injection. The antitoxin levels three months after three injections of the unmodified toxoid compare favorably with the levels of antitoxin in a group of "naturally" immune persons. These results were obtained during a time when the incidence of diphtheria infection was low, as evidenced by the morbidity rates, by carrier studies and by the fact that, among the serums serially titrated, in only five instances was there an indication of a rise in antitoxin level due to secondary stimulus.

Journal of Pharmacology & Exper. Therap., Baltimore

61: 107-204 (Oct.) 1937

Toxicity and Anesthetic Potency of Some Alkoxy Benzoates and Related Compounds. A. R. McIntyre and R. F. Sievers, Omaha.—p. 107.
Effect of Staphylococcus Aureus Exotoxin on Rabbit Heart. J. H. Dingle, H. E. Hoff, L. H. Nahum and B. W. Carey Jr., Boston.—p. 121.
Inhibition of Human Gastric Hypermotility by Atropine or Novatropine. J. P. Quigley, Cleveland.—p. 130.
Hydrolysis of Salts of Barbituric Acids as Related to Rate of Onset of Anesthesia. M. T. Bush, Nashville, Tenn.—p. 134.
Tetra-Alkylbarbituric Acids. M. T. Bush and T. C. Butler, Nashville, Tenn.—p. 139.
Pharmacology of Deuterium Oxide: II. Evidence from Fish Melanophores for Sympathomimetic Action. H. G. Barbour and S. B. Bogdanovitch, New Haven, Conn.—p. 148.
*Further Study of Barbiturate-Picrotoxin Antagonism. J. C. Krantz Jr., C. J. Carr and Frances F. Beck, Baltimore.—p. 153.
Studies of Cyclopropane: III. Relation of Electrocardiographic Changes to Arterial Concentrations of Oxygen, Carbon Dioxide and Cyclopropane in Dogs Anesthetized with Cyclopropane. B. H. Robbins and J. H. Baxter Jr., Nashville, Tenn.—p. 162.
Relative Hypnotic Effects of Some Ureas of Varied Types. A. M. Hjort, E. J. deBeer, J. S. Buck, W. S. Ide and D. W. Fassett, Tuckahoe, N. Y.—p. 175.
Anesthesia with Cyclopropane Derivatives. V. E. Henderson and S. F. MacDonald, Toronto.—p. 182.
*Renal Excretion of Sulfanilamide. E. K. Marshall Jr., K. Emerson Jr. and W. C. Cutting, Baltimore.—p. 191.
*Distribution of Sulfanilamide in Organism. E. K. Marshall Jr., K. Emerson Jr. and W. C. Cutting, Baltimore.—p. 196.

Barbiturate-Picrotoxin Antagonism.—As the work of no previous investigators included a study of oxygen consumption during the period of barbiturate-picrotoxin antagonism, Krantz and his associates studied this phase of the antidotal action. 1. In the white rat picrotoxin significantly antagonizes the depression of oxygen consumption produced by pentobarbital sodium. 2. The increased oxygen consumption produced by epinephrine in normal and in rats depressed with pentobarbital sodium is not effective in antidoting the depressed respiration produced by pentobarbital sodium. Therefore, the antidotal action of picrotoxin against the barbiturates is not primarily an acceleration of oxygen consumption. 3. On the whole rat's brain or on the medullary-pons portion of the rabbit's brain in vitro, picrotoxin fails to combat the depressed potential oxygen uptake, as measured by the rapidity of decolorizing methylene blue solutions. Apparently the antidotal action of picrotoxin is not associated with an increased uptake of oxygen of cerebral tissue in general or cerebral tissue rich in vital centers. 4. Picrotoxin does not apparently stimulate the respiration through the carotid sinus reflex by shifting the acid-base equilibrium of the blood, as the increased respiration occurs without altering significantly the p_H of the blood. Therefore the antidotal action of picrotoxin in barbiturate poisoning is attributable mainly to its convulsive action, referred to by Koppanyi and his assocates as an "awakening effect."

Renal Excretion of Sulfanilamide.—Marshall and his colleagues endeavored to determine the mode of sulfanilamide excretion by the kidney. They studied (1) the clearance of the substance in relation to that of creatinine clearance which presumably measures glomerular filtration, (2) the relation of the plasma concentration of the substance to its clearance and (3) the influence of the rate of the flow of urine on its clearance. In the dog, the sulfanilamide clearance is from 20 to 30 per cent of the simultaneously determined creatinine clearance. If the creatinine clearance is accepted as a measure of the rate of glomerular filtration, from 70 to 80 per cent of the filtered sulfanilamide is reabsorbed in the passage of the glomerular filtrate along the tubule. The sulfanilamide clearance is independent of the plasma concentration of sulfanilamide and is apparently increased by increasing the rate of the flow of urine. Sulfanilamide appears to resemble urea in its excretion in the dog, but to be reabsorbed to a greater extent by the tubule. In a few determinations on man, the average sulfanilamide clear-

ance was 22.5 cc. per minute. If one considers that the inulin clearance in man averages about 125 cc. per minute, it is clear that in man as well as in the dog a large percentage of the filtered sulfanilamide is reabsorbed by the tubule.

Distribution of Sulfanilamide in Organism.—Marshall and his co-workers studied the sulfanilamide content of various tissues and fluids of the body, and the relation of the blood concentration to the total sulfanilamide content of the body. Their results indicate that sulfanilamide is almost equally distributed in the tissues of the organism (with exception of bone and fat) and is probably present in equal concentration in all parts of the body if concentrations are expressed per unit of water.

Medical Annals of District of Columbia, Washington

6: 285-304 (Oct.) 1937

Diagnostic Value of Blood Phosphatase Determination. J. H. Roe, Washington.—p. 285.
Artificial Fever Therapy of Gonorrheal Arthritis. H. B. Gwynn, Washington.—p. 288.
Neurodermatoses. F. J. Eichenlaub, Washington.—p. 293.
Endometriosis: Report of Two Cases. J. K. Cromer, Washington.—p. 295.
*Asthma Following Prolonged Exposure to Sulfur Dioxide: Report of Case. H. F. Dowling, Washington.—p. 299.

Asthma Following Exposure to Sulfur Dioxide.—The inhalation of sulfur dioxide has two possible implications: the immediate toxic effect and the delayed or chronic effect. Since the gas changes into sulfurous acid on contact with water, it is quite irritating to the respiratory passages, its acrid fumes inciting the coughing which is so familiar to those who have performed blood nonprotein nitrogen tests. Inhalation of concentrations of 0.001 per cent by volume causes extreme discomfort, while 0.1 per cent causes death by paralysis of the respiratory center. Refrigerator repairmen are continually exposed to the inhalation of sulfur dioxide throughout each working day. In the case cited by Dowling there were several indications of the allergic state: (1) the history of asthma in his mother, (2) the occurrence of asthma in the patient as a child, (3) the high percentage of eosinophils in the blood and sputum and (4) improvement occurring at the same time as hyposensitization. The patient had an allergic constitution with no clinical symptoms for the previous seventeen years, and inhalation of sulfur dioxide (during his first few days as a refrigerator repairman) acted as an irritant to the respiratory mucosa, permitting the dust allergen to excite asthma as a symptom complex. The pathologic state of the bronchial mucous membrane in asthma offered a favorable medium for the growth of bacteria, and this, together with the continued irritating effect of the sulfur dioxide in lowering the resistance of the bronchial tissues, accounted for the development of the asthmatic bronchitis.

Military Surgeon, Washington, D. C.

81: 321-400 (Nov.) 1937

Death from Cancer, Accelerated by Metastases to Heart: Report of Case. J. R. Darnall.—p. 325.
Gumma of the Muscle. H. B. Cupp.—p. 332.
Identification Through Dental Records. E. J. Ryan.—p. 333.
Malaria at France Field in 1936. H. E. Schneider.—p. 340.
Postarsenical Hemorrhagic Encephalitis: Report of Case. A. H. Hansen.—p. 344.
Mental Hygiene. M. I. Bloomfield.—p. 348.
Human Convalescent Serum in Treatment of Scarlet Fever. J. C. Fox and D. Fisher.—p. 356.
Active Immunization Against Tetanus in Warfare. F. H. Van Wagoner.—p. 365.
Role of Preventive Medicine in Control of Cholera. B. C. T. Fenton.—p. 369.

Minnesota Medicine, St. Paul

20: 691-754 (Nov.) 1937

Use of Sulfanilamide and Prontosil Solution. A. E. Brown, E. G. Bannick and H. C. Habein, Rochester.—p. 691.
Tumors of the Jejunum. J. A. Johnson, Minneapolis.—p. 697.
Significance of Glomerular Nephritis in Childhood. Jessie M. Bierman, Helena, Mont.—p. 703.
Back Injuries as an Industrial Disability. J. R. Kuth, Duluth.—p. 706.
The Adequate and Inadequate Treatment of Injuries of the Head. W. M. Craig, Rochester.—p. 712.
Fracture Dislocation of the Shoulder. H. W. Meyerding, Rochester.—p. 717.
Hand and Wrist Injuries. W. H. Cole, St. Paul.—p. 727.
Injuries of the Thigh. B. S. Adams, Hibbing.—p. 730.
Anal Fissure. W. A. Fansler, Minneapolis.—p. 734.
Transurethral Resection of the Prostate Gland. C. D. Creevy, Minneapolis.—p. 737.

New England Journal of Medicine, Boston

217: 643-686 (Oct. 21) 1937

*Indications for Use of Ammonium Mandelate in Pyuria in Children. W. E. Wheeler, Boston.—p. 643.
Surgical Significance of Melena in Childhood. W. E. Ladd, Boston.—p. 649.
Detection and Measurement of Electrical Concomitant of Human Ovulation by Use of Vacuum-Tube Potentiometer. J. Rock, J. Reboul and H. C. Wiggers, Brookline, Mass.—p. 654.
Progress in Surgery of Autonomic Nervous System. J. C. White, Boston.—p. 660.
Injection-Site Arm Clamp for Self Administration of Insulin. D. L. Davidson, Providence, R. I.—p. 669.

Use of Ammonium Mandelate in Pyuria.—During the last eighteen months, Wheeler has used mandelic acid salts in the treatment of fifty-one patients with acute, chronic or recurrent infection of the urinary tract. Thirty-nine of the patients are free from their urinary infection at present. Infections that are resistant to the action of mandelic acid are fortunately not often encountered in children. If the function of the kidney is good, however, and if there are no severe anomalies, an intensive trial on mandelate therapy may be justified, for some of these infections do clear up under such circumstances. The result of long-standing chronic pyelonephritis in some children, if not successfully treated, is a hypertensive state which may terminate in uremia. The knowledge of this not too uncommon end result of chronic infection should encourage one to employ the best methods available to control urinary infections in their initial stages and prevent them from becoming deep seated and chronic. Successful results may be expected in a large proportion of patients if there is good bilateral renal function, if the patient is in the afebrile stage at the time of treatment, if there are no obstructive anomalies of the urinary tract, and if the details of treatment are followed carefully.

Northwest Medicine, Seattle

36: 333-370 (Oct.) 1937

Neglected Professional Duties. D. C. Ray, Pocatello, Idaho.—p. 333.
Acute Lower Abdomen in the Female. N. F. Miller, Ann Arbor, Mich.—p. 334.
Progress in Pediatrics. D. M. Dayton, Tacoma, Wash.—p. 338.
Suction Pressure Treatments in Impaired Circulation of Extremities. Lucy Hobson, New York.—p. 342.
Oxygen and Carbon Dioxide Therapy: Basic Principles and Practical Applications. G. A. Dodds and C. R. Jensen, Seattle.—p. 345.
Infection Treated with Sulfanilamide. W. D. Clark, Battleground, Wash.—p. 349.
Spinal Anesthesia, with Especial Reference to Dosage. H. S. Atwood, Yakima, Wash.—p. 350.
Ligation of Internal Saphenous Vein: Outline of Varicose Vein Treatment. E. A. Nixon, Seattle.—p. 352.

Ohio State Medical Journal, Columbus

33: 1069-1188 (Oct.) 1937

Useful Hints in Treatment of Gastro-Intestinal Disease. W. C. Alvarez, Rochester, Minn.—p. 1085.
Splenectomy in Relation to Disorders of Blood. R. L. Haden, Cleveland.—p. 1093.
*Artificial Fever Therapy of Sydenham's Chorea. H. W. Kendell and W. M. Simpson, Dayton.—p. 1097.
Rupture of the Uterus. D. J. Davies, Cincinnati.—p. 1101.
Pneumococcic Meningitis, Type II, with Recovery: Due to Hyperthermia? R. W. Frankmann and J. V. Stewart, Massillon.—p. 1105.
Some Clinical Aspects of Arthritis. W. A. McConkey, Canton.—p. 1108.
Significance of Pyuria. J. K. Nealon, Newark.—p. 1114.
Treatment of Carcinoma of Bladder by 400 Kilovolts Roentgen Therapy. A. H. Schumacher and D. Steel, Cleveland.—p. 1116.
Protamine Insulin and Diabetic Children. S. D. Edelman and R. I. Fried, Columbus.—p. 1119.
Interpretation of Serum Tests in Artificially Sensitized Man: Report of Cases Giving Accelerated Reactions with Negative Tests. I. L. Levin, Lorain.—p. 1121.

Artificial Fever Therapy of Sydenham's Chorea.—Kendell and Simpson have subjected five patients suffering from Sydenham's chorea to artificial fever therapy, using the Kettering hypertherm. All experienced prompt cessation of choreiform movements. None have had recurrence. There were four females and one male. The duration of chorea prior to administration of artificial fever ranged from ten days to three weeks in the four severe cases, and in one mild case there had been repeated attacks for one year before artificial fever therapy was given. These patients were given from one to eleven treatments, the average single fever session being three hours between 104 and 105 F. The period of observation extends

from six weeks to four and one-half years. In addition to the choreiform movements, three patients showed evidence of carditis as demonstrated by mitral murmurs, electrocardiographic changes and tachycardia. The mitral murmurs disappeared in all following treatment. The normal cardiac rate and rhythm was restored. Two patients had polyarticular arthritis, which also responded promptly to artificial fever. No other form of treatment was employed in these cases. All the children tolerated the treatments well; none were injured in any way by the artificial fever treatments.

Oklahoma State Medical Assn. Journal, McAlester

30: 351-390 (Oct.) 1937

"Regimented Rationale" in Treatment of Rheumatic Disease. W. K. Ishmael and E. D. McBride, Oklahoma City.—p. 351.
Value of Localizing Reactions in Atrophic or Chronic Infectious Arthritis: Nonspecific Type. E. Goldfain, Oklahoma City.—p. 359.
Ectopic Pregnancy. H. G. Crawford, Bartlesville.—p. 362.
Appendicitis in Children. M. J. Searle, Tulsa.—p. 366.
Tumors of the Jaws. J. F. Burton, Oklahoma City.—p. 369.
Treatment of Gonorrhea in the Male. D. W. Branham, Oklahoma City.—p. 374.

Pennsylvania Medical Journal, Harrisburg

41: 1-78 (Oct.) 1937

Acute Appendicitis in Infants. P. A. McCarthy, Philadelphia, and J. L. Magrath, Upper Darby.—p. 5.
Insulin Shock Therapy in Schizophrenia. F. J. Braceland and D. W. Hastings, Philadelphia.—p. 7.
Successful Treatment of Schizophrenia in a General Hospital: Résumé of Technic Employed. C. Rea and C. M. Kershner, York.—p. 14.
*Tetanus with Total Hemolysis: Report of Case. W. E. B. Hall, St. Joseph, Mo.—p. 16.
The Modern Approach to Early Diagnosis in Tuberculosis: Illustrated by a Case Finding Campaign in 12,000 Pennsylvania School Children. S. O. Pruitt, Philadelphia.—p. 22.
Primary Carcinoma of Duodenum. J. O. Woods, New Castle.—p. 27.
Retrotracheal Thyroid: Case Report. J. A. Soffel, Pittsburgh.—p. 31.
Etiologic and Diagnostic Study of 200 Ward Patients. J. C. Doane and M. S. Jacobs, Philadelphia.—p. 33.
Acute Osteomyelitis of Lumbar Vertebrae: Report of Case. J. S. Donaldson, Elizabethtown.—p. 36.
The Present Conception of Anemia: Relation of Hypoproteinemia to Macrocytic Anemia. H. M. Ray, Pittsburgh.—p. 39.

Tetanus with Total Hemolysis.—Hall cites a case of total blood hemolysis, following the intravenous injection of tetanus antitoxin serum, in a young girl exhibiting symptoms of tetanus eleven and one-half days after a firecracker burn which had necessitated administration of prophylactic serum. At the time of hospitalization the girl was found not to be sensitive to the serum, but she was desensitized as a precaution. The explanation is believed to be (1) a hemolysin release through a replaced amboceptor-antiamboceptor combination in the presence of amboceptor sensitization, the serum antilysin acting as the amboceptor, (2) an unusual specific Arthus reaction through red cell fixation of sensitizing hemolysin-antihemolysin elements or (3) a combination of the two.

Psychiatric Quarterly, Utica, N. Y.

11: 531-716 (Oct.) 1937

Position of Occupational Therapist in a Plan of Research in Schizophrenia. N. D. C. Lewis, New York.—p. 537.
Psychiatric Implications in Occupational Therapy. L. E. Hinsie, New York.—p. 544.
Dementia Praecox: Preventable. P. Milici, Kings Park, N. Y.—p. 552.
Intracranial Neoplasms: Their Incidence and Mental Manifestations: Study Based on Clinical and Autopsy Records of 2,000 Patients at St. Elizabeths Hospital. J. L. Hoffman, Washington, D. C.—p. 561.
Streptococcic Meningitis with Recovery in Case of General Paresis. I. M. Derby and M. Zeifert, Brooklyn.—p. 576.
Epileptic Psychosis: Clinical Study. I. Schnap, Kings Park, N. Y.—p. 582.
The Psychology of Headache: Case Studied Experimentally. Jule Eisenbud, New York.—p. 592.
Racial Variation in Blood Cerebrospinal Fluid Barrier of Normal Children. F. A. Mettler, M. Robinow, H. G. Stelling, C. M. Burpee and M. K. Amdur, Augusta, Ga.—p. 620.
Objective Signs of Invalidity of Stanford-Binet Tests. Z. A. Piotrowski, New York.—p. 623.
Report on Tuberculosis Survey Recently Completed at Marcy State Hospital. D. A. Harrison, Utica, N. Y., and G. Schein, Marcy, N. Y.—p. 637.
Fire Prevention in State Hospitals. C. W. Hutchings, Marcy, N. Y.—p. 643.
Studies in Obsessive Ruminative Tension States: V. Etiology, Dynamics and Genesis of Psychasthenia. L. F. Woolley, Towson, Md.—p. 654.
Technical Approaches Used in Study and Treatment of Emotional Problems in Children: Part V. The Playroom. J. Louise Despert, New York.—p. 677.

Public Health Reports, Washington, D. C.

52: 1473-1518 (Oct. 22) 1937

Studies on Oxyuriasis: VI. Incidence of Oxyuriasis in 1,272 Persons in Washington, D. C., with Notes on Diagnosis. Eloise B. Cram, Myrna F. Jones, Lucy Reardon and Mabelle O. Nolan.—p. 1480.

South Carolina Medical Assn. Journal, Greenville

33: 229-254 (Oct.) 1937

Practical Points in Treatment of Coronary Disease. L. T. Gager, Columbia.—p. 229.
Psychoneurosis Following Injury. C. O. Bates, Greenville.—p. 233.
Synopsis of Congenital Hemolytic Jaundice: Preliminary Report of Two Cases in Identical Twins. P. H. Culbreath, Ellenton.—p. 238.

33: 255-280 (Nov.) 1937

The Physician and the Public Health. L. Banov, Charleston.—p. 255.
Some Observations on Osteomyelitis of Maxilla in Infants: Report of Case. J. W. Jervey Jr., Greenville.—p. 258.
What Does Your Profession Mean to You? C. B. Epps, Sumter.—p. 262.

Southwestern Medicine, Phoenix, Ariz.

21: 339-376 (Oct.) 1937

Care of the New-Born. M. K. Wylder, Albuquerque, N. M.—p. 339.
Therapeutic Value of Iodized Oil Intratracheally in Bronchiectasis. R. M. Balyeat, Oklahoma City.—p. 341.
*Diagnosis of Blood Dyscrasias and Allied Diseases. H. Jeter, Oklahoma City.—p. 343.
Cervix and Some of Its Problems. J. H. Patterson, Phoenix, Ariz.—p. 348.
The Present Management of Cancer of Rectum. W. H. Daniel, Los Angeles.—p. 352.
Treatment of Skin Cancer. E. C. Fox, Dallas, Texas.—p. 354.
Chronic Fluorine Intoxication: Report of "Mottled Enamel" in a Dog. R. deR. Barondes, San Francisco.—p. 357.
Gonorrhea: Treatment and Its Inadequacy: Gonococci Acquired by New-Born in Nose, Mouth, Urethra and Vagina, as Well as Eyes: Gonococci Seem to Cause Arthritis and Rheumatism: Are Gonococci, Like Syphilis, Passed on to the Third and Fourth Generations? G. S. Chapin, Los Angeles.—p. 363.

Diagnosis of Blood Dyscrasias and Allied Diseases.—Jeter mentions certain aids in the diagnosis, management and treatment of blood dyscrasias and allied diseases. Routine bone marrow biopsy is probably not indicated but should be made in cases in which other hematologic studies do not lead to satisfactory diagnoses. Neutropenia of various degrees and associated with various conditions are frequently observed. Neutropenia has been found in typhoid, malaria, poisoning from heavy metals, roentgen and radium therapy, panhypoplasia of the bone marrow associated with aplastic anemia, and various other conditions. The reticulocyte count by a special vital stain has become necessary in the study of anemias. Syphilis is frequently in the background in occult anemia and, if the diagnosis can be established and antisyphilitic treatment instituted, recovery is more complete than could be expected by symptomatic treatment of the anemia. Acute, subacute and chronic nephritis has been observed to be an obscure cause of obvious anemia. Other chronic diseases such as tuberculosis, diseases of the gastro-intestinal tract, particularly amebiasis, polyposis and diverticulitis fall into this group. In simple achlorhydric anemia (so-called chronic microcytic anemia and sometimes called idiopathic hypochromic anemia), if no clue to the etiology can be established and achlorhydria is present along with a normal quantity and quality of leukocytes and thrombocytes, large doses of iron and hydrochloric acid are administered. The results are frequently most spectacular. The diagnosis of hemolytic jaundice, or the so-called congenital familial icterus, is established by chronicity, history of heredity, icterus, splenomegaly, increased fragility of erythrocytes and high reticulocyte count, and recently, as pointed out by Haden, the erythrocytes tend to be more spheroid in character than in any other type of anemia. The sickle cell trait which occurs in a certain percentage of normal Negroes is not to be confused with sickle cell anemia. Chlorosis is conspicuous because of the extreme low color index and the characteristic color of the skin. In the author's experience syphilis, chemical poisoning, roentgen therapy and, occasionally, chronic low grade infections are the causes of aplastic anemia. Too frequently the aplasia of the bone marrow is a terminal condition and elimination of the cause is too late. Hemorrhagic purpura is often, if not always, a syndrome of symptoms with characteristic changes in the blood secondary to some ordinarily obscure primary condition.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Bristol Medico-Chirurgical Journal

54: 191-238 (Autumn) 1937

Nutrition and Tuberculosis. J. A. Nixon.—p. 191.
Burden Mental Research Trust: Its Present and Future. R. J. A. Berry.—p. 201.
Sulfanilamide in Treatment. E. Watson-Williams.—p. 209.
Prontosil in Obstetrics. H. J. Drew-Smythe.—p. 217.
Ham Green Hospital Extensions: The Opening Address Delivered on September 23, 1937. W. W. Jameson.—p. 221.

British Journal of Physical Medicine, London

12: 115-138 (Oct.) 1937

Value of Ultraviolet Light in Industrial Districts. Eva Morton.—p. 117.
Impedance of Human Body to Direct Current and Low Frequency Alternating Current. W. E. Boyd and M. R. Gavin.—p. 119.
Constant Galvanic Current. A. P. Cawadias.—p. 125.

British Journal of Radiology, London

10: 701-764 (Oct.) 1937

Some Abnormalities of Pharynx, Esophagus and Diaphragm (Including Diaphragmatic Hernia). T. P. Dunhill.—p. 702.
Radiation Dosimetry: Part II. L. H. Gray.—p. 721.
*Congenital Undescended Cecum. A. C. Jordan.—p. 743.
(I) A Nomogram for Radiography; (II) an Exposure Calculator for Radiography. A. B. MacLean.—p. 753.
A Compact Neon-Tube Radium Detector. P. R. Pallister.—p. 759.

Congenital Undescended Cecum.—Jordan states that congenitally undescended cecums include at least five varieties: 1. The cecum that has descended as far as the upper part of the right iliac fossa; the ascending colon hangs down vertically, then turns vertically up to the hepatic flexure, thus forming a letter J. 2. The cecum that has descended as far as the front of the right kidney; the ascending colon forms a U, with the right limb shorter than the left. 3. The cecum the descent of which is arrested at some point along the lower border of the liver; the ascending colon forms a U with equal limbs; the hepatic flexure is a little farther to the left than normal. 4. The cecum that, instead of moving to the right from its earliest epigastric position, descends in the middle line, remaining well forward and free from attachments (hence very mobile), leaving the whole right side of the abdomen to the small intestine. 5. The cecum that remains in its earliest position, high in the epigastrium, well forward, in front of the lower part of the duodenum. The congenitally undescended cecum causes a high degree of ileac stasis, while the cecum is less fully loaded than normal; this is different from the usual state of affairs in stasis. It is well that the surgeon should realize fully what he is likely to encounter in such a case; the terminal ileum will have no peritoneal covering and no mesentery.

British Medical Journal, London

2: 731-782 (Oct. 16) 1937

Cholecystitis. J. W. McNee.—p. 731.
Cholecystography: Efficiency of the Graham-Cole Test. T. G. Hardman.—p. 733.
Magnesium Trisilicate. N. Mutch.—p. 735.
*Tuberculosis of Cervical Lymphatic Glands. R. Reid and M. C. Wilkinson.—p. 740.
Relation of Blood Group of the Individual to Blood Diseases and Neoplasms. K. I. E. Macleod.—p. 745.

Tuberculosis of Cervical Lymphatic Glands.—While Reid and Wilkinson recognize that different methods may be employed with excellent results by different workers, they outline a method of treatment based on the pathology of tuberculosis of the cervical lymphatic glands that has achieved a fair measure of success in 119 consecutive cases. The treatment consisted of a combination of constitutional and operative measures; but constitutional treatment has been the fundamental factor, and in no case was surgical extirpation of the tuberculous glands adopted as a primary measure. The cases were divided into three groups (1) enlarged glands with periadenitis, (2) enlarged glands without periadenitis and (3) cases of residual infection following natural or artificial attempts at cure. Tuberculous lymphadenitis may be regarded as a local tuberculous lesion in a patient whose resistance to the disease is insufficient. Constitutional treatment, therefore, is of paramount importance to prevent progress or recrudescence of the disease. The chief factors in constitutional treatment are rest (restraint from all activity), open air, a liberal balanced diet with an adequate supply of vitamin and heliotherapy. Tonsillar and pharyngeal sepsis in the pathology of tuberculous glands of the neck is of utmost importance. The treatment of a tuberculous abscess arising from a gland depends on whether superadded secondary infection has occurred or not. If there is secondary infection the pus should be evacuated by incision, and free drainage should be established. If there is no secondary infection an attempt should be made to treat the abscess by aspiration. The success of aspiration depends on the employment of a technic in which the needle is passed into the cavity of the abscess through and across muscle. The route of the needle is thus closed by the approximation of the muscular fibers. The operation for radical excision of tuberculous glands of the neck is a controversial field in surgery. The main contraindication for the operation is active disease with periadenitis. The group 1 cases treated by conservative means required on an average 6.7 months to complete a clinical cure, and twenty-four of twenty-nine gave a good result on discharge. The operative forty-five cases were under general treatment for an average period of 2.9 months before they passed from this group to group 2 or 3, and were then ready for operation. After operation one month of treatment was given to allow satisfactory healing of the wound. There were good results in all the operative cases. Satisfactory results were obtained in the six cases in group 2 under constitutional treatment. They were retained in the sanatorium for an average period of 3.25 months. The sixteen cases treated by operation all gave good results and were kept under constitutional treatment for an average period of two months before operation. The statistics of the thirteen cases in group 3 give no useful information, as the group contains such a variety of cases of residual infection that no generalization can be made about them. But the immediate results following treatment in all groups were good except in five cases of group 1. Ten patients did not complete the treatment. It is the authors' opinion that the nasopharyngeal lymphatic tissue is the probable path of entry for the tubercle bacillus in this disease. Tuberculosis of the cervical lymph glands is a local disease which does not give rise to metastatic lesions.

Lancet, London

2: 781-834 (Oct. 2) 1937

Reflections on the Health Campaign. Dawson.—p. 781.
Deafness: Prevention versus Palliation. A. Tumarkin.—p. 782.
Gold Treatment of Arthritis: Review of 900 Cases. S. J. Hartfall, H. G. Garland and W. Goldie.—p. 784.
*Inquiry into "Relapse" Following Sympathectomy. H. T. Simmons and D. Sheehan.—p. 788.
Bacteriostatic Action of p-Aminobenzenesulfonamide on Hemolytic Streptococci. H. Finklestone-Sayliss, C. G. Paine and L. B. Patrick.—p. 792.
Electrocardiographic Changes of a T_2 Pattern in Pericardial Lesions and in Stab Wounds of the Heart. P. Wood.—p. 796.
Effects of Thyrotropic Hormone of Anterior Pituitary in Man. E. F. Scowen.—p. 799.

"Relapse" Following Sympathectomy.—In a series of patients in whom the cervicothoracic ganglion had been removed or its preganglionic fibers divided, Simmons and Sheehan studied the effect of sweating tests, ulnar nerve block and the administration of dilute epinephrine intravenously. The results do not support the explanations of the cause of relapse after sympathectomy offered by Lewis in England and White in America. It has been found that the relapse coincides with the reappearance of vasoconstrictor fibers in the ulnar nerve. It is suggested that regeneration of sympathetic fibers must explain their reappearance.

Chinese Medical Journal, Peiping

52: 317-478 (Sept.) 1937

Edema in Pregnancy. W. C. W. Nixon.—p. 317.
Blood Pressure in Pregnancy. L. Ride.—p. 329.
Treatment of Kala-Azar with Solustibosan: A New Antimony Compound. E. B. Struthers and L. C. Lin.—p. 335.
"Sdt. 561" in Treatment of Kala-Azar. T. M. Yates.—p. 339.
Salmonella Infection: Study of Seventeen Cases of Salmonella Enteritidis Septicemia. C. H. Huang, H. C. Chang and V. T. Lieu.—p. 345.

Journal de Médecine de Lyon

18: 549-576 (Oct. 20) 1937

*Treatment of Pulmonary Tuberculosis with Gold Salts. P. Courmont, H. Gardère and P. Rivollier.—p. 549.
*Mode of Action of Gold Salts in Pulmonary Tuberculosis. P. Courmont and H. Gardère.—p. 559.

Treatment of Pulmonary Tuberculosis with Gold Salts.—Courmont and his associates point out that the opinions about the efficacy and the method of the treatment of tuberculosis by means of gold salts are contradictory. This is partly due to the fact that the statistics are not comparable as regards the selection of the cases, the type of gold preparation that is employed, the method of treatment and so on. The authors present observations on a material in which these factors were the same. They report about 117 adults from the same clinical department. Only one type of gold salt was used and the preparation was administered intravenously in doses of 0.1 Gm. Among thirty-four patients in whom the treatment was completed, the temperature was reduced in 56 per cent of the cases, the weight was increased in 57 per cent; the sputum was reduced in 50 per cent, the bacilli disappeared in 44 per cent, there was roentgenologic improvement in 25 per cent and the mortality was 23 per cent. On the other hand, in the fifty-four patients who did not receive the gold therapy and in the twenty-nine in whom the treatment was not completed, the corresponding figures were extremely unfavorable and the mortality was twice as high as in the treated group. The favorable action of the treatment cannot be disputed. The authors never observed a severe accident. To be sure, they administered only small doses and strictly adhered to certain rules. In a series of sixty-eight cases they observed twenty-nine with mild and generally early complications, but these accidents by themselves never caused serious consequences. The treatment was at once stopped in the twenty-nine cases as soon as the complications developed. It is of great interest to note that in the patients who developed these early complications the mortality was twice as high as in those in whom the treatment was completed, and the improvements were small in number. As all these cases were in the beginning entirely comparable to those which were submitted to the complete treatment, it may be deduced that the extreme sensitivity to the first injections of the gold preparation indicates that the general resistance of these patients is much lower. From this the authors draw the conclusions that (1) it is inadvisable to continue the gold treatment in these sensitive patients and (2) that the prognosis is quite often unfavorable in the sensitive patients. These points and the loss of weight are the most important ones to be watched in the course of the treatment. The authors remain advocates of the small doses which produce good results and are not followed by grave accidents; the mild reaction which they may elicit makes it possible to determine the sensitivity of the patients.

Mode of Action of Gold Salts in Pulmonary Tuberculosis.—Courmont and Gardère show that the study of the mode of action of gold salts in pulmonary tuberculosis is of great importance, because a knowledge of the action mechanism is a guide in conducting the treatment and helps to avoid grave accidents. This action mechanism is complex. Factors that must play a part are (1) the bactericidal power of the gold salts and the increase in the natural bactericidal power of the organism (serum urine), which was proved by experiments, (2) the reticulo-endothelial system and the organs, such as liver and spleen, which contain much of this tissue and (3) the focal reactions against the tuberculous lesions. These reactions must remain slight to be useful; if they do not, they provoke complications. The use of small doses (0.05 or 0.1 Gm. per week) seems sufficient to induce and sustain the beneficial reaction with the least complications. The pathogenesis of the accidents is likewise extremely complex. They may be due to intoxication (too strong or accumulated doses) with toxic lesions of the liver and kidney, to idiosyncrasy (unforeseen, spontaneous sensitivity), or to sensitization acquired by the injections. The mode of action of this sensitization is still being disputed. It is made evident in certain cases by cutaneous tests and by passive sensitization. An important part is played by the general hypersensitivity of the tuberculous organism produced by the tuberculosis itself, which influences all those processes and accidents. The authors conclude that all these processes are complex and interrelated, that extreme caution is necessary in the use of gold salts, that it is advisable to administer only small doses, and that the treatment should be stopped as soon as complications develop.

Paris Médical

2: 317-328 (Oct. 23) 1937

*New Sign of Appendicitis: Contraction of Adductors of Right Side. C. Richet and H. Netter.—p. 317.
Cardiac Aspects of Prolonged Malignant Endocarditis. D. Olmer and A.-X. Jouve.—p. 319.
*Anemia in Course of Prolonged Treatment with Barbituric Preparation in Epileptic Patients: Several Cases. G. Maillard and Mlle. Jammet.—p. 325.

Contraction of Adductors as Sign of Appendicitis.—Richet and Netter point out that of all the physical signs of appendicitis the most evident is contraction. According to the cases it is located solely or chiefly in the right iliac fossa, in the lumbo-iliac space, above the crural arch, under the liver, sometimes on the left side, sometimes generalized. Occasionally it is the psoas that is contracted. But whatever may be the severity of the appendicitis, there often exists the contraction of the adductors of the right thigh, which is easily made evident. The patient is lying on the back with the mouth open, thighs half flexed, heels flat on the bed and knees touching; the muscular relaxation must be complete. Placing a hand or, better, a finger on the internal edge of each knee, one exerts a pressure directed from within outward, tending to separate the knees one from the other and to press them down with their external surface on the bed, as if one attempted the limitation of the abduction in a beginning coxalgia. It is necessary to use a mild pressure constantly and equally on the two sides. This maneuver is not painful. Exceptionally it is possible to detect an intense contraction of the adductors of the right thigh, the member remaining in an almost vertical plane, while the left knee is easily pressed outward. Nearly always there is a slight contraction, a simple hypertonia, the abduction being less marked on the right than on the left; at the same time there is a sensation of an opposing resistance of the member, which one feels better in repeating the maneuver once or twice, but always with lightness. If the manipulation is made with force, the result is always negative. One of the authors has systematically searched for this sign and has detected it in about 40 per cent of the cases of appendicitis. The hypertonia of the adductors of the right thigh is especially frequent in the acute forms of appendicitis. It is found with equal frequency in adults and in children. The sign has symptomatologic value, because systematic search for it in other disorders on the right side of the abdomen never revealed it. In doubtful cases it has often made it possible for the authors to decide the diagnosis in favor of an appendicitis. In attempting to explain the sign, the authors direct attention to the motor innervation of the adductors.

Anemia in Course of Treatment with Phenobarbital.—Having observed anemia in two epileptic patients who had been treated for a long time with phenobarbital, Maillard and Jammet examined the blood of fifteen epileptic patients who had been treated with phenobarbital for several years. In eight of these patients they detected a more or less severe reduction in erythrocytes and also other changes. The authors describe the hemograms of these patients and state that the symptoms of anemia are often latent in these patients, so that the existence of the anemia is disclosed only by an examination of the blood. The anemia could be counteracted by reducing the dose of phenobarbital and by treating the patients with liver extract.

Jahrbuch für Kinderheilkunde, Basel

150: 1-64 (Sept.) 1937

Treatment of Rickets with Concentrated Viosterol. H. Bischoff.—p. 2.
*Significance and Prognosis of Spontaneous Pneumothorax During Childhood. H. Wissler.—p. 11.
Syndrome Accompanied by Generalized True or Spurious Platyspondylia. J.-R. Dreyfus.—p. 42.

Spontaneous Pneumothorax During Childhood.—On the basis of fifty-seven cases observed, Wissler discusses the clinical significance and the prognosis of spontaneous pneumothorax. He found that in the majority of cases the pneumothorax developed in the course of a pneumonia, usually in the form of a pyopneumothorax. In two instances the spontaneous pneumo-

thorax developed without apparent cause. In these cases of idiopathic, benign spontaneous pneumothorax; no inflammatory disorders of the lung existed; the clinical course was mild and complete recovery followed. Approximately two thirds of the cases of total pneumothorax and pyopneumothorax terminated in death, regardless of whether puncture had preceded the development of the pneumothorax or not. This indicates that the previous pleural puncture is of no significance for the prognosis. In the cases of partial pneumothorax the mortality was considerably less than in those of total pneumothorax, in that only about one seventh of the cases terminated in death. In nearly all cases in which necropsy was done, an abscess-forming pneumonia could be detected. In severe cases, particularly in small children, the development of a pneumothorax can be taken as an indication of this form of pneumonia. In approximately one half of the cured cases a tension pneumothorax existed for a long time. These cases, which the author describes in detail, indicate that a considerable excess of pressure is tolerated. The unfavorable course in the other cases was chiefly the result of the primary disorder. The pneumothorax is an undesirable complication, but it does not determine the outcome. The encapsulated pneumothorax has a more favorable prognosis than has the total pneumothorax. Its significance lies in the diagnostic difficulties it may cause, particularly in the differentiation from conditions with similar roentgenologic aspects, such as pulmonary abscess, tuberculous cavity, postpneumonic pseudocavity and bronchiectatic cavity. The differential diagnosis is discussed on the basis of several cases.

Folia Medica, Naples

23: 901-970 (Sept. 15) 1937

*Hyperostosis of Internal Aspect of Frontal Bone. M. Raso.—p. 903.
Workers in Sulfur Mines in Sicily. S. Frazzetto.—p. 947.

Hyperostosis of Internal Aspect of Frontal Bone.—Raso performed necropsies in thirteen cases of hyperostosis of the internal aspect of the frontal bone (Morgagni syndrome). The condition is more frequent in women than in men and, in the present group, was associated with virilism in only one case and with obesity in another. None of the patients suffered from hypophysial or endocrine disorders. The microscopic picture varies according to the phase of evolution of the condition when the patient dies. When the pathologic process is in evolution there is an intense development of fibrous connective tissue all through the thickness of the frontal bone, which is followed by formation of active osteoblasts. When the process is established, evolution stops and reabsorption of the bone, which is characteristic of old age, takes place. The author reviews the etiopathogenic theories which trace the disease to endocrine disorders, cerebral atrophy, formation of adhesions between the meninges and the bone, disorders of the calcium metabolism, pathologic local disorders as shown by Paget, inflammation and disorders of general and local circulation. He believes that local inflammation, secondary to that of the paranasal pneumatic cavities, and local circulatory disturbances are the most plausible etiopathogenic factors.

Archivos Arg. de Enf. del Ap. Digest., Buenos Aires

12: 573-674 (Aug.-Sept.) 1937

*Atypical Chronic Appendicitis: Maneuver for Diagnosis. D. Del Valle and A. Giordano.—p. 573.
Surgical Biopsy in Hepatobiliary Diseases. R. E. Donovan and A. C. Aguirre.—p. 581.
Functional Compensation in Large Resection of Digestive Tract. J. C. Bidart Malbrán, A. Giordano and S. Garelick.—p. 599.
Hectic Fever in Cancer of Stomach. C. Boronino Peró, A. Richieri and J. C. Blaskley.—p. 614.
*Gastric Secretory Function and Its Relation to Acid Base and Sodium Chloride Equilibrium. H. J. d'Amato, H. E. Bordo and J. Scopp.—p. 622.
Perforated Ulcer of Duodenum Complicated by Pulmonary Abscess Cured by Short Wave Treatments. L. Ayerza and J. L. A. Mulcahy.—p. 630.
Infra-Ampullar Primary Carcinoma of Duodenum. J. A. Pangaro and N. Sirven.—p. 639.

Atypical Chronic Appendicitis.—Del Valle and Giordano say that the atypical forms of chronic appendicitis show symptoms of gastric diseases, colitis or cholecystitis without any pain, spontaneous or induced by palpation on the right iliac fossa. Their maneuver for diagnosis of the condition consists in a gentle massage over the iliac fossa, which is performed for a few minutes while the patient's abdominal muscles are in relaxation and then repeated for two or five consecutive days. The presence of pain on first examination of the patient contraindicates massage. It may indicate presence of diseases other than appendicitis which can be aggravated by massage. If atypical or chronic appendicitis is present, pain at the McBurney point appears in the course of the treatment, spontaneously or during palpation. It points to the advisability of performing an appendectomy. After the massage the febricula and the number of leukocytes increase and a paracecal pain appears. As a rule the appendix shows inflammation. The gastric and other symptoms from which the patient complained disappear after appendectomy. The authors report two cases of a group of twenty in which the satisfactory results of appendectomy persist after ten years.

Gastric Secretion, Acid-Base Equilibrium and Chlorides.—D'Amato and his collaborators say that the gastric secretion induces a change of the balance between the acid-base equilibrium and the chlorides in the blood. During the first two hours after the ingestion of food the chlorides in the blood plasma diminish while the bicarbonates and the alkali reserve increase. After the second hour, in the process of digestion, the reaction of the blood shifts to acidosis as a result of the loss of alkali radicals through the bile and duodenal and intestinal juices. The amount of chlorides eliminated through the secreting glands of the gastric mucosa is larger than that in the blood. This fact is due to an organic reaction of compensation by which the tissues deliver chlorides to the blood as the latter delivers chlorides to the secreting glands of the gastric mucosa. Administration of merbaphen induces mobilization of the chlorides from the tissues to the blood. The amount of chlorides in the gastric secretion which was stimulated by administration of an alcohol meal is larger in patients who are taking a dechloridated diet or a diet containing a small amount of sodium chloride than in those who are having a normal diet. The increase, however, lasts only for one hour, after which the chlorides in the gastric secretion are normal. A dechloridated diet or one which contains a small amount of sodium chloride regulates neither the amount of chlorides nor the acidity of the gastric secretion. It induces hyperchloremia during the period of digestion only during the first few days, after which a permanent hypochloremia is established.

Semana Médica, Buenos Aires

44: 857-912 (Oct. 14) 1937

*Elastic Thoracoplasty. R. Finochietto and H. Aguilar.—p. 857.
Venereal Granuloma. E. P. Fidanza and F. R. Ruiz.—p. 863.
Attempted Induced Abortion: Perforation of Uterus and Prolapse of Epiploon, Continuation of Pregnancy After Operation. J. B. González.—p. 883.
Bengal Red Test in Study of Liver Function. A. C. Grapiolo and D. Cavanna.—p. 886.

Elastic Thoracoplasty.—Finochietto and Aguilar's paravertebral (para-osteal) resection of the first three ribs by posterior approach aims to induce elastic thoracoplasty. The technic is as follows: The patient lies in the lateral position on the normal side, slightly ventrad, with a small cushion under the axilla of the normal side and the arm of the side of the tuberculous lung resting easily in front of the thorax. The incision begins at a point 3 or 4 cm. below the upper edge of the trapezius muscle, runs downward over the scapulovertebral space, paralleling the spinal edge of the scapula, at a distance of 2 or 3 cm., and turns slightly outward at the inferior angle of the scapula. The trapezius and rhomboideus muscles and the cellular tissues of the scapulothoracic space are incised and retracted. The anterior serratus muscle is sectioned at a point 10 or 12 mm. from its costal insertion and the small tendons of the muscles which are attached to the spinous processes are dissected one by one at a point 2 or 3 mm. from their insertion. Paracostal resection is done first on the third rib, then on the second and at last on the first one. A weak solution of procaine hydrochloride or of sodium chloride is injected in the intercostal space and at the lower edge of the rib to be resected. Slightly traumatized fragments of the intercostal muscles remain adhering to the pleura and are harmless. If the third rib was sectioned up to the anterior axillary line an axillary drainage is left. If it was sectioned at the posterior axillary line the drain is paravertebral. The operation causes no shock and gives satisfactory results.

Beiträge zur pathologischen Anatomie, Jena

100: 1-194 (Oct. 1) 1937. Partial Index

State of Irritation. L. Aschoff.—p. 1.
*Osteitis Fibrosa and Parathyroids in Animal Experiment. W. Eger. —p. 19.
Modification of Shape of Facial Portion of Skull by Premature Unilateral Ossification of Coronal Suture. A. Materna.—p. 42.
Allergic-Hyperergic Appendicitis. K. Heinemann.—p. 62.
Question of Calcium Deposits in Giant Cells. K. Zäh.—p. 126.
*Connection Between Pineal Body and Adrenal Cortex. J. von Kup.—p. 137.
White Pulmonary Infarct: Pathogenesis and Further Development. F. Niendorf.—p. 149.
Formal Genesis of Congenital Micrognathia. A. Giordano.—p. 169.

Osteitis Fibrosa and Parathyroids in Animal Experiment.—Eger shows that by inducing chronic lead intoxication in rats it is possible to elicit changes in the bones that can be compared with osteitis fibrosa in human subjects. The changes in the bones are accompanied regularly by an enlargement of the parathyroids. This enlargement of the parathyroids seems to be a secondary manifestation in a primary disturbance of the metabolism.

Connection Between Pineal Body and Adrenal Cortex.—Von Kup gives the clinical history of a boy, aged 3½ years, who exhibited physical, mental and particularly sexual prematurity, which apparently was connected with a hyperfunction of the adrenals or with the endocrine sequels of this hyperfunction. The boy died shortly after the extirpation of a large (830 Gm.) malignant adenoma of the left adrenal cortex. The necropsy revealed changes in the endocrine glands. There was an enlargement of the hypophysis. The pineal body, however, was subnormal in weight. In the pancreas there was hyperplasia of the glandular parenchyma to the detriment of the insular apparatus. The weight of the testes was increased. There was a generalized hypertrichosis. The author shows that the clinical history of the boy corresponds with the pathologic anatomic aspects and permits the following conclusions: There is a close, morphologically demonstrable connection between the function of the adenohypophysis and that of the adrenal cortex. The hyperfunction of the adrenal cortex and the endocrine results of this condition caused an increase of weight of the adenohypophysis. The author has previously pointed out that there is an antagonism between the adrenal cortex and the pineal body and, as is well known, between the pineal body and the adenohypophysis. The antagonism between adrenal cortex and pineal body becomes manifest by way of the antagonism between the pineal body and the adenohypophysis; that is, hyperfunction of the adrenal cortex causes enlargement (and evidently hyperfunction) of the adenohypophysis, which in turn exerts an inhibiting effect on the development of the pineal body. To the hyperfunction of the adenohypophysis must be ascribed the premature development of the gonads and with this the sexual prematurity. Thus there is also an indirect connection between the adrenal cortex and the gonads. The observations described here are corroborated by cases previously described and by animal experiments.

Münchener medizinische Wochenschrift, Munich

84: 1561-1600 (Oct. 1) 1937. Partial Index

*Further Experiences on Treatment of Massive Gastric Hemorrhages Without Restriction of Diet. E. Meulengracht.—p. 1565.
Treatment of Pneumonia with Vitamin C. A. Vogl.—p. 1569.
*Danger of Anesthesia of Mucosa of Injured Male Urethra. R. Knepper. —p. 1572.
Oral Sepsis: Case. L. Walb.—p. 1573.
Nonspecific Antitoxic Treatment of Infectious Diseases. W. Stoeltzner. —p. 1573.
Bandage for Hallux Valgus. H. Schwan.—p. 1580.

Treatment of Gastric Hemorrhages. — Meulengracht reports that since 1931 he has treated massive gastric hemorrhages without restriction of diet. His experiences with this method of treatment were made in 368 cases of hematemesis or melena, resulting from acute or chronic ulcers. He found that the hemorrhage was not exacerbated when immediately thereafter the patients were given as much food as they desired. The diet is a puréed one and the patients are given five meals daily. In addition they receive alkalis, atropine and iron. The patients are permitted to move in bed as much as they desire. Under the influence of this treatment the subjective condition of the patients is much better than under the former treatment with a gradually increasing ulcer diet. The patients regain their strength rapidly, regeneration of the blood sets in promptly and the convalescence is shortened. Intake of food into the stomach does not exacerbate the hemorrhage. The mortality from gastric hemorrhage was greatly decreased by this treatment.

Danger of Anesthesia of Injured Male Urethra.—Knepper points out that, although in case of an intact mucosa there is no toxic effect from the anesthetic which is introduced previous to cystoscopy, severe or even fatal intoxications have been known to occur in case of an injured mucosa of the urethra or when the mucosa was injured by the pressure of the syringe. It is characteristic for such cases that the signs of intoxication and even death follow rapidly; that is, almost immediately after the toxic substance enters the blood stream. This proves that the intoxication is the result of the direct entrance of the anesthetic into the blood stream; that is, there is practically an intravenous injection of the anesthetic. This is due to the fact that a true submucosa is absent in the mucosa of the urethra and a venous plexus is directly underneath the mucosa. Consequently, any injury that reaches below the mucosa involves an opening of the venous system. The author reports the history of a man, aged 57, who died immediately after anesthesia of the urethra. The necropsy revealed defects in the mucosa near a postgonorrheal urethral stricture and there was evidence that the anesthetic had entered the venous system of the corpus cavernosum. He admits that pressure might play a part in the involuntary injection into the urethral venous plexus, but he thinks that an anesthetic of the consistency of a thin fluid will enter openings into the venous system even in the absence of pressure. For this reason he decided to introduce the anesthetic in the form of a thick fluid. He recommends the following prescription: tragacanth 0.75 to 0.1; glycerin 10; pantocain 0.5 to 0.1; distilled water to 50. Anesthetization is begun ten minutes before cystoscopy and is entirely adequate for the intervention. The viscous character of the anesthetic not only prevents it from entering possible breaches in the urethral mucosa but also facilitates easy passage of the cystoscope.

Wiener Archiv für innere Medizin, Vienna

31: 113-168 (Sept. 30) 1937

Blood Sugar and Water Thrust. A. Visani.—p. 113.
Blood Pressure Reaction and Cold Stimulation. H. Brada and L. Feil.—p. 121.
*Etiology of Menstrual Hemoptysis. A. Sattler.—p. 129.
*Occurrence of Weil's Disease in Vienna. R. Fleckseder.—p. 139.
Partial Pulmonary Collapse. K. Strässler.—p. 155.

Menstrual Hemoptysis.—Sattler points out that it is well known that hemorrhages from the lung are especially frequent at the time of menstruation in women with pulmonary tuberculosis. Discussing the causes of the menstrual hemoptysis, the author describes a typical case. Repeated severe hemoptyses at the time of menstruation finally made an intervention necessary, which proved that adhesions which suspended a pulmonary cavity in the pneumothorax space and the enormous hyperemia of the lung and pleura at the time of menstruation were the chief causes of the menstrual hemoptysis. A control thoracoscopy during the intermenstrual period revealed that the severe hyperemia of the lung and pleura had subsided. From this observation the author concludes that a causal connection exists between excessive blood perfusion of the lung and the menstrual process.

Weil's Disease in Vienna.—Fleckseder gives detailed histories of three out of six patients with Weil's disease who recently came up for observation in two Viennese hospitals. The first patient was a man, aged 42, who frequently fished in the river and who had sustained slight abrasions while doing so. Following this he had Weil's disease with the typical fever curve, severe hepatic impairment, icterus, hemorrhagic diathesis and acute renal disorders with polyuria during the period when the fever subsided. The serum of the patient agglutinated Spirochaeta icterogenes with a titer of 1:1,000. This case ended in recovery, but the other two had a fatal outcome. Both of the latter patients had been working on canals. In analyzing these cases and in reviewing the literature, the author noted a similarity between Weil's disease and another spirochetal disease, namely, recurrent fever, cases of which he had observed during the war. In both disorders the following symptoms may appear: backache, muscular pains, particularly pains in the calves of the legs, severe cerebral symptoms, even delirium, severe conjunctival congestion and iritis, also recurrent periods

of fever, which apparently are connected with the life cycles of the two types of spirochetes. However, there are differences as well as similarities. For instance, in recurrent fever the splenic tumor is more pronounced than is the case in Weil's disease. The behavior of the causal agents differs in that in Weil's disease they are less numerous in the blood and in recurrent fever they are less numerous in the urine. Then there are differences as regards the morphology, serologic reaction and the animal pathogenicity. The author considers the differential diagnosis between Weil's disease and various forms of toxic icterus, pylephlebitis, cholangitis and so on and discusses the prevention of the disease. He points out that physicians and nurses who take care of patients with Weil's disease, and laboratory workers who handle materials from such patients, must be extremely careful: the latter should wear rubber gloves and eye protectors. In view of the fact that Weil's disease is disseminated by rats, attention should be given to the extermination of rats in canals, slaughter houses, markets and mines. For persons who are especially exposed to infection, such as canal workers, the author recommends protective vaccination with killed spirochetes.

Wiener medizinische Wochenschrift, Vienna

87: 1099-1126 (Oct. 23) 1937

*Cardiac Defects During Childhood. A. F. Hecht.—p. 1099.
Clinical Aspects of Hypophysial Diseases. W. Raab.—p. 1103.
Trachea and Aorta. S. Kreuzfuchs.—p. 1106.
Medicinal Shock Therapy of Schizophrenia. M. Sakel.—p. 1108.

Cardiac Defects During Childhood.—Hecht discusses the present status of the diagnosis and treatment of cardiac defects in children. He cites two cases in which the cardiac disturbance was of traumatic origin, both being cases of cardiac concussion. He points out that the second case is of especial interest to physicians supervising athletic activities. Further he takes up the various forms of endocarditis, particularly rheumatic endocarditis and the valvular insufficiencies. He says that it is best to begin the treatment of new endocarditis with an energetic medication with salicylic acid, but that good results have been obtained also with aminopyrine. Treatment with digitalis is usually not advisable in endocarditis. In the myocardial defects electrocardiography is often helpful. To be sure, there are cases in which the electrocardiogram remains normal to the fatal end. On the other hand, electrocardiographic changes that develop in the course of diphtheria, scarlet fever and influenza are often reversible. The arrhythmias are discussed. It is pointed out that extrasystoles may occur in the absence of functional impairment. Disturbances in the stimulus conduction system are always a partial manifestation of cardiac defects. Pericarditis presents no unusual features during childhood. The congenital cardiac defects are usually characterized by severe cyanosis. In the latter the treatment is only symptomatic. Following a discussion of some symptoms of cardiac insufficiency, namely, dyspnea, hepatic swelling and edemas, the author evaluates strophanthin and digitalis therapy. Then he discusses the use of diuretics and the dietetic therapy of edemas. If hydrothorax, ascites and hydropericardium are accompanied by severe disturbances in compensation, they necessitate puncture; severe edemas yield only to capillary drainage. If such severe cases develop during childhood, the prognosis as regards life expectancy is much more unfavorable than if it develops in later life.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

81: 4919-5018 (Oct. 16) 1937. Partial Index

Pathogenesis of Cancer of Corpus Uteri. I. A. Wijsenbeek.—p. 4926.
*Heredity of Albinism. J. Sanders.—p. 4932.
*New Points of View in Experimental Cancer Research. A. L. Hagedoorn and A. C. Hagedoorn.—p. 4938.
Eclampsia. D. G. Wesselink.—p. 4950.

Heredity of Albinism.—Sanders reports that questionnaires sent to ophthalmologists disclosed 216 cases of albinism in 140 families. Investigations on this material revealed that the heredity of albinism is of the monorecessive type. The author directs especial attention to two families in which both the dominant albinismus circumscriptus and the recessive albinismus totalis were present. He thinks that these heterozygotes are an exception to most heterozygotes, since these are nearly always phenotypically normal.

New Points of View in Research on Cancer.—The Hagedoorns show that in most cases in which hereditary developmental factors influence a disease it is found that one single gene is more or less the determining factor. In mice, cases of cryptorchidism, anemia, deafness and other disorders were found to follow this rule. However, carcinoma of the mammary gland of mice is an exception. In cross breeding experiments between strains with and without cancer, it was found that the female offspring of the females of the group with cancer develop cancer, whereas the female offspring of the males of the same strain do not. From these observations, Little and Korteweg draw the conclusion that this is a case of extrachromosomal heredity. However, repeated back crossings with males of the cancer strain finally result in the production of females that do develop mammary cancer, a fact which contradicts the aforementioned conclusion. The authors direct attention to experiments in which it was shown that the animals of the cancer strains do not thrive well, that they are poor mothers and that the young grow poorly. The only way to raise the young to normal, healthy mice was to have them suckled by normal mice. Many of these fostering experiments confirmed the hypothesis that cancer of the breast is induced by the fact that the young mice are suckled by females of the cancer strains. In the females of a cancerous strain which were suckled by their mothers, the incidence of cancer was 83.2 per cent, but in females of the same strain which were suckled by normal animals the incidence of cancer was only 4.9 per cent. Moreover, some young females of strains that were free from cancer later developed cancer when they had been suckled by females of the cancerous strain. The authors suggest experiments that will reveal whether cancer is produced by the presence in the milk of a cancer inducing substance or by the lack of an important substance. They conclude that the so-called hereditary factor in cancer of the breast can be counteracted by a simple intervention during early childhood.

Hygiea, Stockholm

99: 705-736 (Oct. 15) 1937

Remarks on Gastric Hypachylia and Achylia, Treatment and Complications. E. Forsgren.—p. 705.
*Further Remarks on Anorectal Stricture in Venereal Lymphogranuloma. G. Redell.—p. 713.

Anorectal Stricture in Venereal Lymphogranuloma.—Redell's patient, an ex-sailor, aged 32, with rectal stricture and venereal lymphogranuloma, had had marked symptoms of colitis for four years; the administration of Frei antigen intravenously, according to Hellerström, was followed by remarkable improvement. An earlier case of anorectal stricture on the basis of venereal lymphogranuloma in which satisfactory results were obtained by this method of treatment was reported by the author in *Hygiea* **98:**417 (July 15) 1936.

Ugeskrift for Læger, Copenhagen

99: 993-1016 (Sept. 23) 1937.

*Chronic Acetophenetidin Intoxication: Utilization of Blood in Acetophenetidin Cyanosis; Ventilation of Question of Liver Cirrhosis on Basis of Protracted Intoxication with Aniline Derivatives. T. Espersen.—p. 993.
Experiences with Ergotamine Tartrate in Migraine. A. Guldager.—p. 999.

Acetophenetidin Intoxication.—Espersen reviews cases of chronic acetophenetidin intoxication from the literature, discusses the different conceptions of the cause of cyanosis in intoxication with aniline derivatives and reports a case of fatal chronic acetophenetidin poisoning in a woman, aged 30, who for three years had taken 1.5 Gm. of acetophenetidin daily (in all, between 1,600 and 1,700 Gm.). He says that spectroscopy, about three weeks after the last dose of acetophenetidin, showed neither methemoglobinemia nor sulfhemoglobinemia. Determination of the oxygen capacity according to Van Slyke and Hiller, about four weeks after the last intake of acetophenetidin, revealed no decrease in active oxygen binding in spite of constant cyanosis, and the arteriovenous oxygen difference was normal. The conception is thus supported that the cyanosis depends on the presence of dark oxygenized para-amidophenol combinations. The liver cirrhosis found post mortem is probably to be interpreted as a result of the long-continued acetophenetidin intoxication.